Carbohydrates

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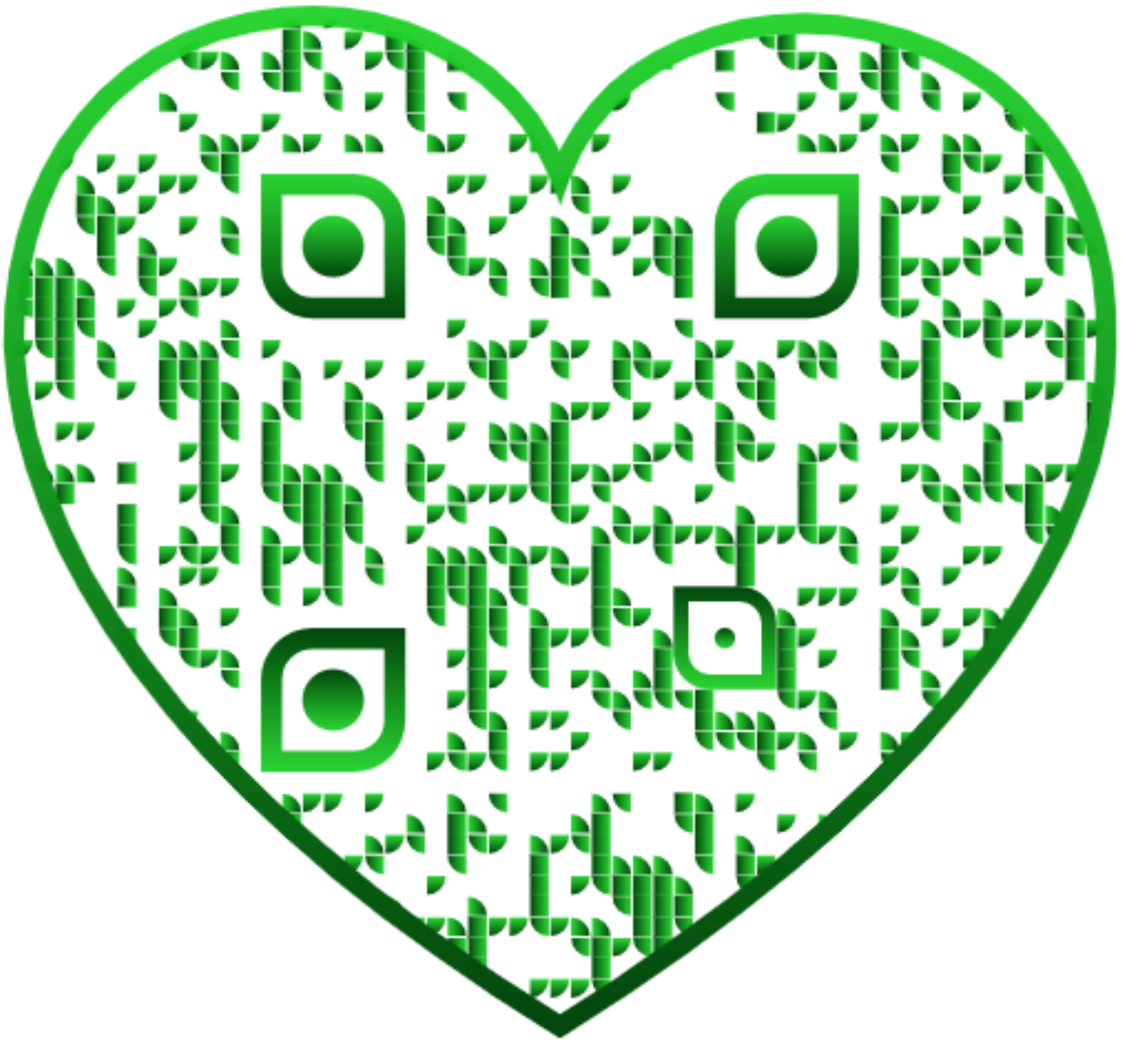


Introduction

- Carbohydrates are defined chemically as aldehyde or ketone derivatives of the higher polyhydric alcohols, or compounds which yield these derivatives on hydrolysis.
- Carbohydrates are also said to be saccharides (Latin, saccharon, sugar)

Introduction…

- Carbohydrates constitute a major class of naturally occurring organic compounds.
- They include such as sugars, starch and cellulose.
- They are essential to the maintenance of life in both plants and animals.
- They provide raw materials for many important industries including textiles, artificial silks, paper, films, plasters, drugs, fermentation and explosives.

Introduction…

- Carbohydrates as the name implies are composed mainly of carbon, hydrogen and oxygen with the latter two elements in the ratio of 2 to1as in water.
- These compounds may be represented by general formula Cx(H2O)y, where x and y may be same or different.
- For ex. We can write glucose C6H12O6 as C6(H2O)6
- Because of this fact they were considered in the early days to be hydrates of carbon and for thus reason were called carbohydrates.

Introduction…

- Some carbohydrates such as rhamnose ($C_6H_{12}O_5$), do not contain the usual proportions hydrogen and oxygen.
- Further more some carbohydrates are now known which contain nitrogen or sulphur in addition to carbon, hydrogen and oxygen.
- Structurally carbohydrates are polyfunctional compounds.

Introduction…

- They contain two types of functional groups, the hydroxyl group and the carbonyl group.
- They are polyhydroxy aldehydes or plyhydroxy ketones or compounds which are converted to these on hydrolysis.

- The formation of carbohydrates in nature occur in green plants by a process called photosynthesis.
- Plants contain the green pigment chlorophyll which catalyzes the conversion of carbon dioxide and water into sugar.
- There action is the thermodynamically unfavourable but proceeds because the necessary energy is supplied by the sun in the form of light.

- $6CO_2 + 6H_2O +$ <u>solar energy</u> $C_6(H_2O)_6 + 6O_2$
- While plants build up carbohydrates from carbon dioxide and water, animals degrade carbohydrates by eating plants and combine the carbohydrates with oxygen from the air to carry out the reverse of photosynthesis.

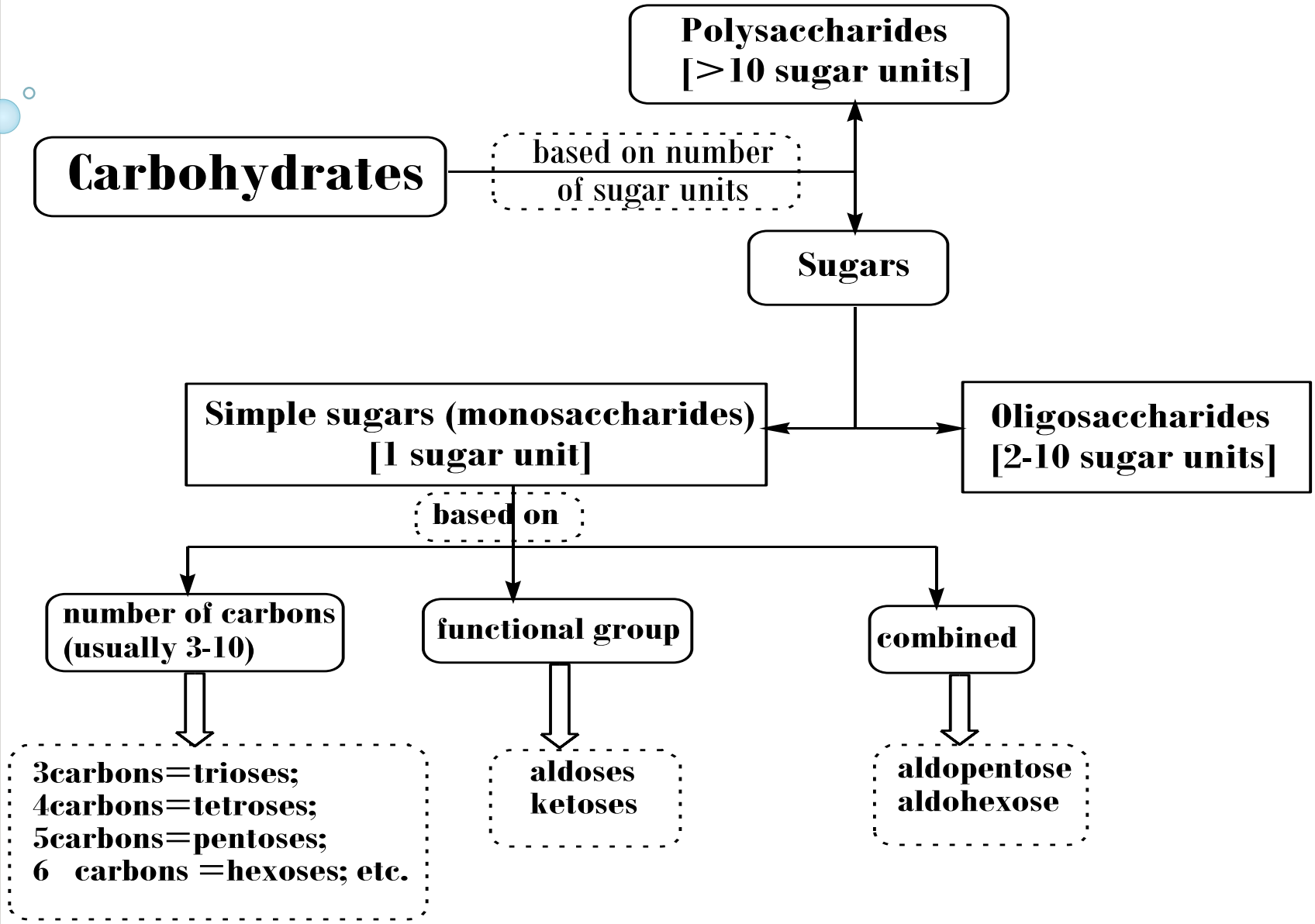
Classification of carbohydrates

- Most of carbohydrates are characterized by the ending "-ose".
- Thus we have glucose, fructose, sucrose, cellulose and soon.

Carbohydrates can be divided as:

- **Sugars**, which are Simple, mainly crystalline, sweet, and soluble in water
- **Polysaccharides**, which are Mainly non-crystalline (amorphous), not sweet, and less soluble or insoluble in water

II. Classification



Carbohydrates cont.

- SUGARS
  - ✓ are colorless crystalline compounds
  - ✓ have sweet taste
  - ✓ are soluble in water
  - ✓ have low molecular weight
- POLYSACCHARIDES
  - ✓ are amorphous solids
  - ✓ are tasteless
  - ✓ are generally insoluble in water
  - ✓ have high molecular weight

- **The carbohydrates are divided into three major classes depending upon whether or not they under go hydrolysis**:

A. Monosaccharides, which are polyhydroxy aldehydes or polhydroxy ketones which cannot be decomposed by hydrolysis to give simpler carbohydrates.

- Examples: Glucose and fructose, both of which have molecular formula, $C_6H_{12}O_6$.
- $C_6H_{12}O_6 + H_2O \xrightarrow{H^+}$ No Reaction
- **Monosaccharaides a**re the simplest sugars that cannot be hydrolysed into smaller units.

- **Mono saccharides** in turn subdivided:

i. based on the type of functional group

- ✓ **Aldose**–if it contains an aldehyde group (-C-H) e.g., **glucose** have an aldehyde group at one end and
- ✓ **Ketose**-if it contains acetone group (C)e.g., **fructose** have a keto group, usually at C-2

- **ii. Based on the number of carbons it contains**
- **Triose** (when it contains 3 carbon atom),
- **Tetrose** (when it contains 4 carbon atom),
- **Pentose** (when it contains 5 carbon atom),
- **Hexose** (when it contains 6 carbon atoms) and so on

B. Oligosaccharides

- Oligosaccharides (greek,oligo,few) are carbohydrates which yield a definite number(2-9) of monosaccharide molecules on hydrolysis.
- Are sugars that can be hydrolysed into two to nine units (molecules)

They include,

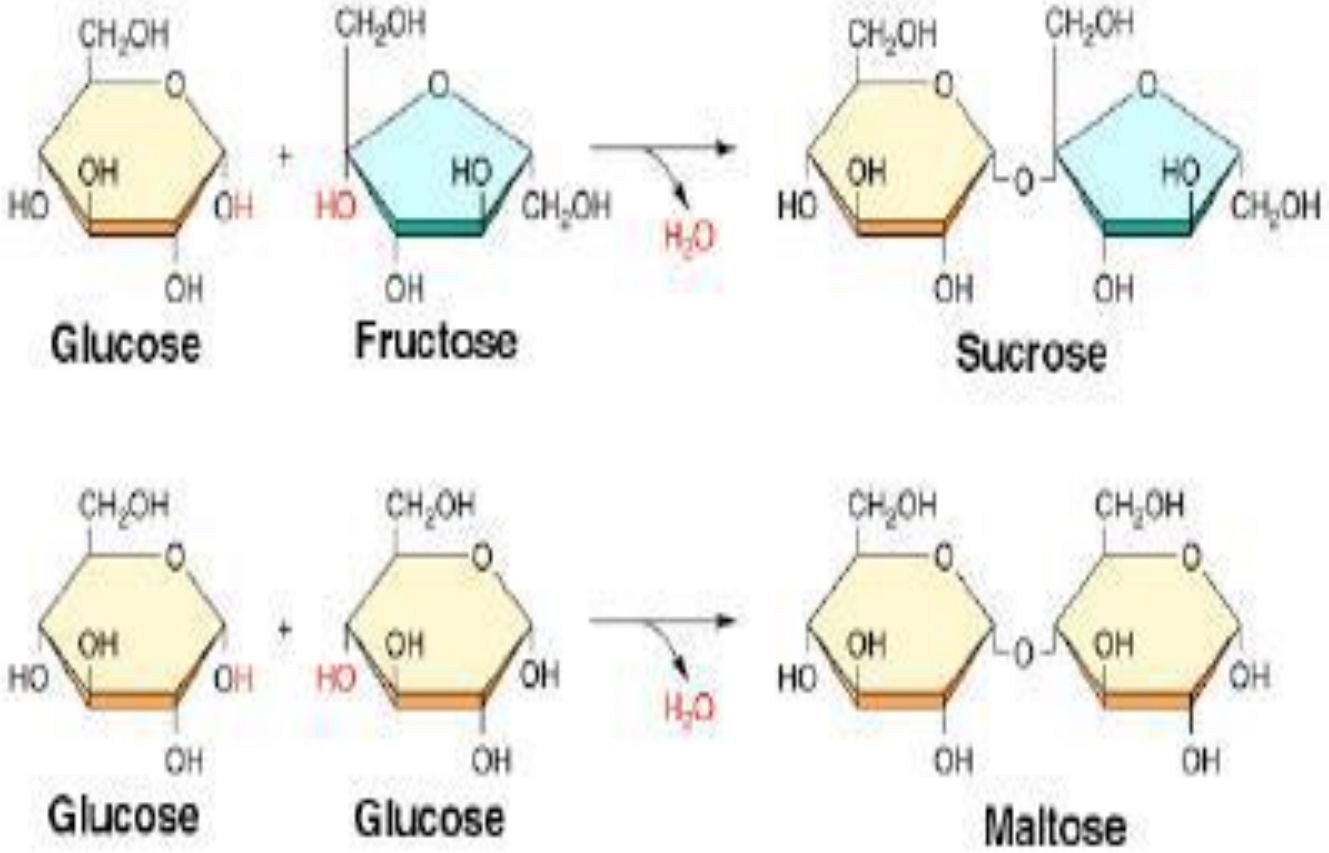
I. Disaccharides-are hydrolysed to two sugar units
II. Trisaccharides- are hydrolysed to three sugar units
III. Tetrasaccharides- are hydrolysed to four sugar units etc.

(i). Disaccharides yield two monosaccharide molecules on hydrolysis.

- ☐Examples are sucrose and maltose, both of which have molecular formula $C_{12}H_{22}O_{11}$.

- $C_{12}H_{22}O_{11}$(sucrose) + H_2O $\xrightarrow{H^+}$ $C_6H_{12}O_6$ + $C_6H_{12}O_6$
  glucose fructose

- Disaccharides are 2 monosaccharides joined by a dehydration synthesis, or condensation, which is removal of a water molecule.
- The“H” is taken from a hydroxyl functional group of one monosaccharide and the “OH” from the second. The two molecules are then joined by a C-O-C bond.


Glucose
Fructose
Sucrose
Glucose
Glucose
Maltose

(ii) Trisaccharides yield three monosaccharide molecules On hydrolysis.

- Example is raffinose, which has molecular formula C18H22O16.

- $C_{18}H_{22}O_{16}$(raffinose) + $2H_2O$ $\xrightarrow{12H^+}$ $C_6H_{12}O_6$ + $C_6H_{12}O_6$ + $C_6H_{12}O_6$
  glucose fructose galactose

C . Polysaccharides

- The polysaccharides are carbohydrates of high molecular weight which yield many monosaccharide molecules on hydrolysis.
- Examples are starch and cellulose, both of which have molecular formula, $(C_6H_{10}O_5)_n$.

$$(C_6H_{10}O_5)_n + nH_2O \xrightarrow{H^+} nC_6H_{12}O_6$$

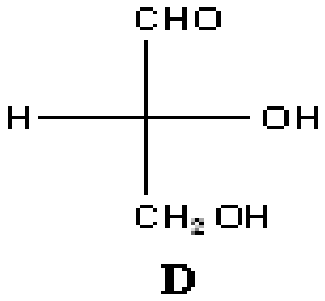
Starch or cellulose ⟶ glucose

Carbohydrates cont.

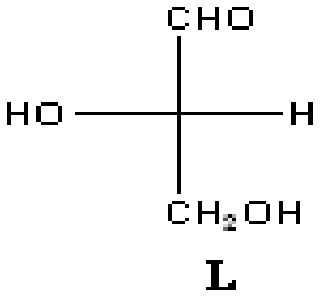
III. Reactions and configuration of monosaccharide's

1. Stereochemistry and structure of monosaccharides

- ✓ Stereochemistry of carbohydrates began in about 1900
- ✓ X-ray crystallography started in about 1957
  - Until that the absolute configuration of compounds was not possible
  - Fischer used a convention to assign the configuration of glyceraldehyde



D



L

D-Glyceraldehyde, when the OH is to the right; L-Glyceraldehyde, when the OH is to the left

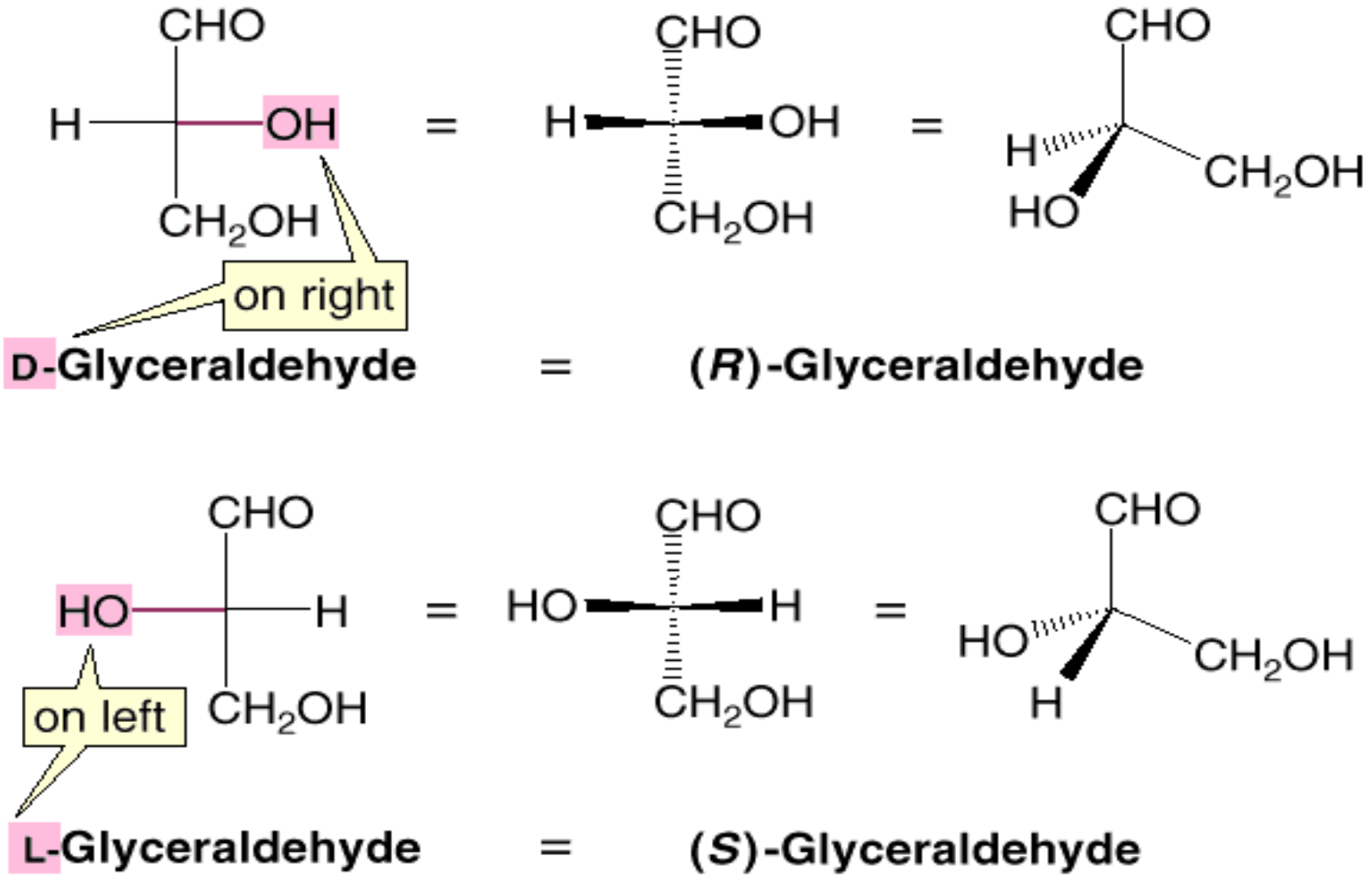
Stereochemistry and structure cont.

- ✓ D & L designations are based on the configuration about the single asymmetric carbon in glyceraldehyde.
- ✓ For sugars with more than one chiral center, D or **L** refers to the asymmetric **C** farthest from the aldehyde or keto group.
- ✓ Other constituents can be compared depending on whether they are or not on the same side of the OH assigned previously
- ✓ This type of configuration is called the **relative configuration**

Stereochemistry and structure cont.

- Thus, books written before 1957, tell the relative configuration and not the absolute configuration of compounds
- Glyceraldehyde is an aldotriose because it has a three-carbon backbone and an aldehyde group.

Stereochemistry and structure cont.



The two enantiomers of the simplest sugar, glyceraldehydes

Reactions and configuration cont.

2. Nomenclature and Structure of monosaccharides

- Aldo sugars are written with the aldehyde group at the top and the primary alcohol at the bottom.
- In this scheme, called a **Fischer projection**, horizontal bonds are taken as coming toward the viewer and vertical bonds as retreating.

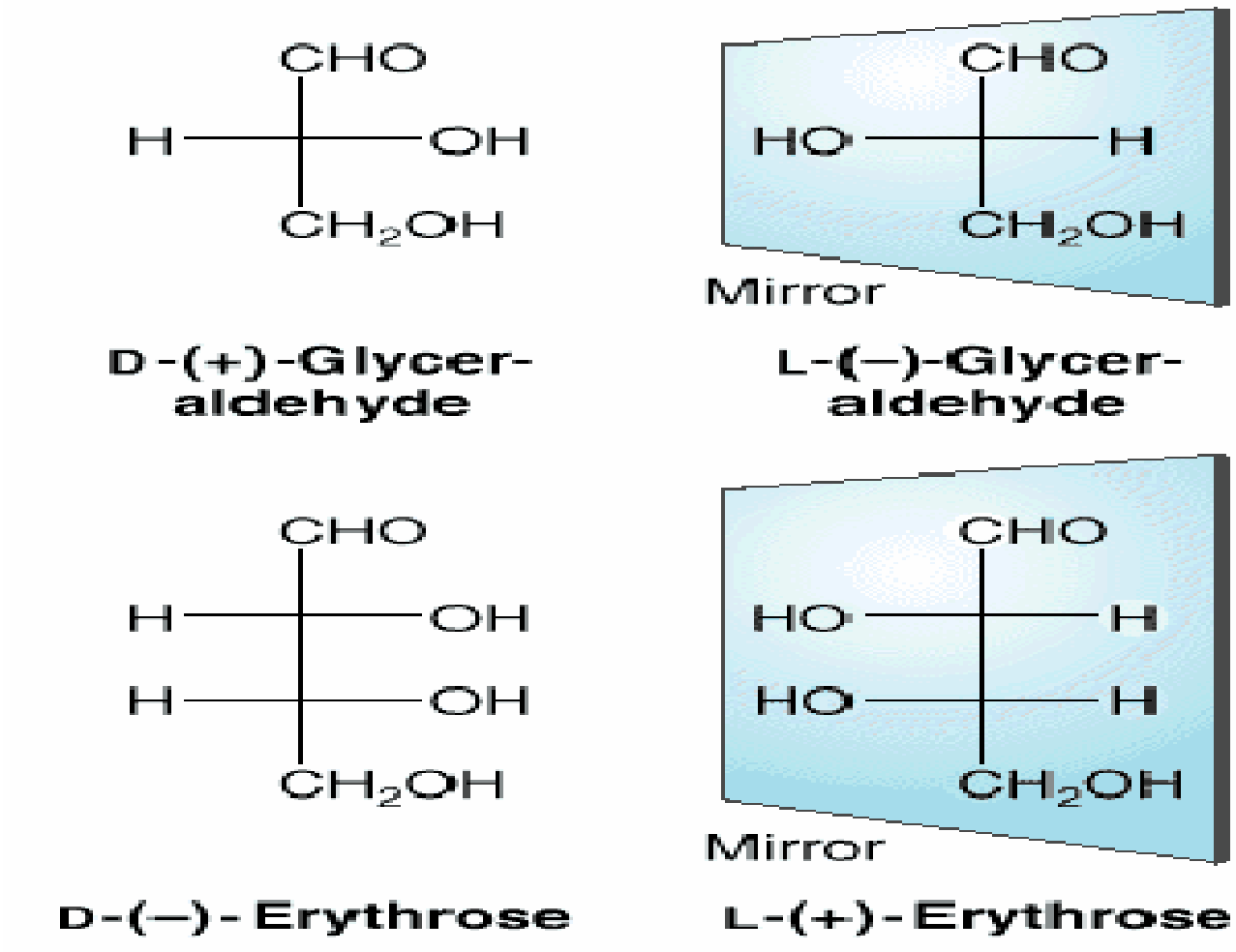
Nomenclature and Structure cont.

- If the OH adjacent to the primary alcohol at the bottom is
  - ✓ on the right, the sugar is a member of the **D series**
  - ✓ on the left, it is in the **L series**.
- Most naturally occurring sugars are D isomers.
- D & L sugars are mirror images of one another. They have the same name, e.g., D-glucose & L-glucose.

Nomenclature and Structure cont.

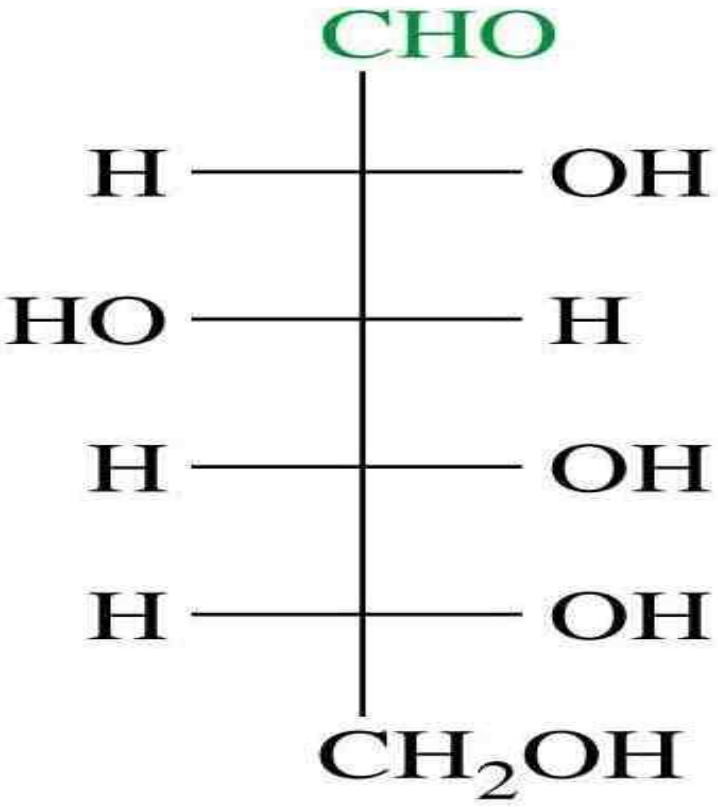
- Other stereoisomers have unique names, e.g., glucose, mannose, galactose, etc.
- The number of stereoisomers is 2^n, where n is the number of asymmetric centers.
- The 6-C aldoses have 4 asymmetric centers. Thus there are 16 stereoisomers (8 D-sugars and 8 L-sugars).
- There is no relation between D and L and the sign of optical rotation, (+) and (-).

Nomenclature and Structure cont.

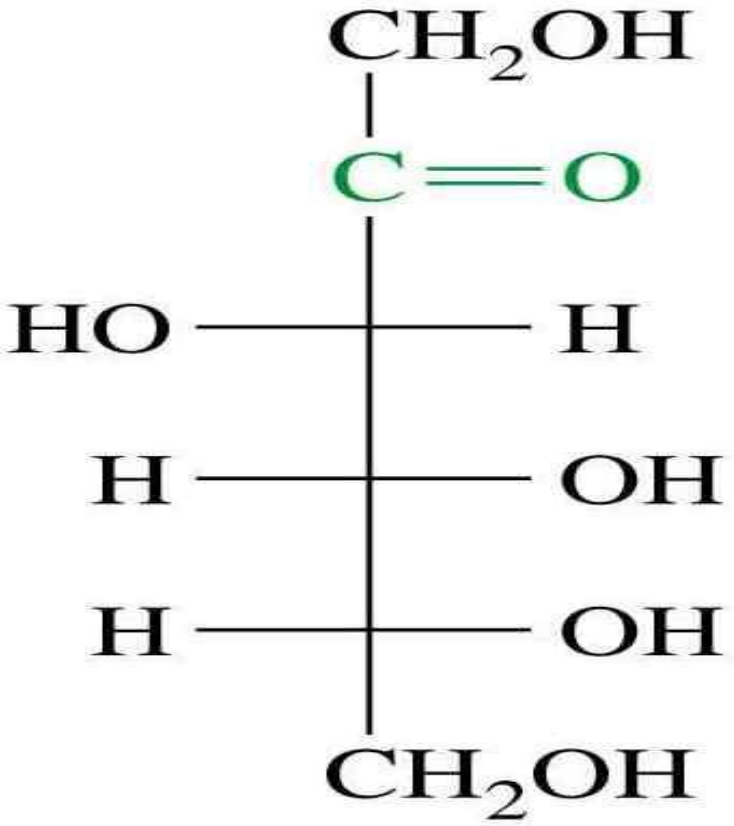


No relation between D and L and the sign of optical rotation, (+) and (-).

Nomenclature and Structure cont.

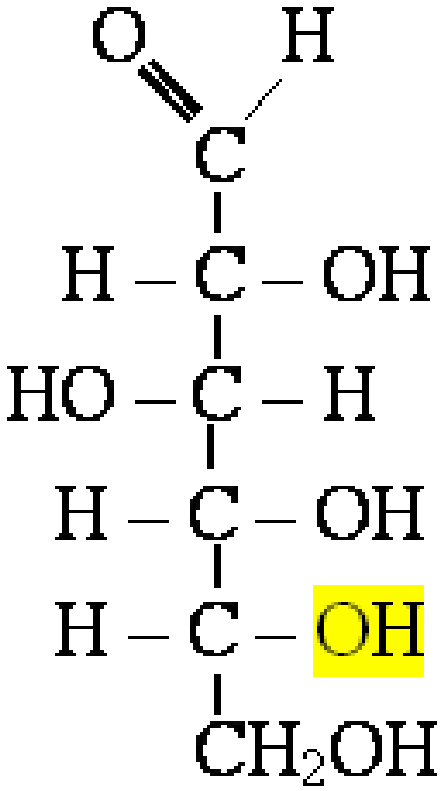


Glucose (a D-aldohexose)

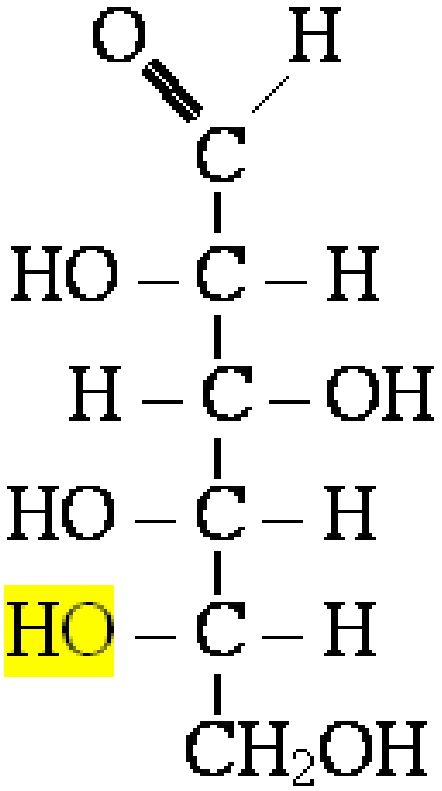


Fructose (a D-ketohexose)

Nomenclature and Structure cont.



D-glucose

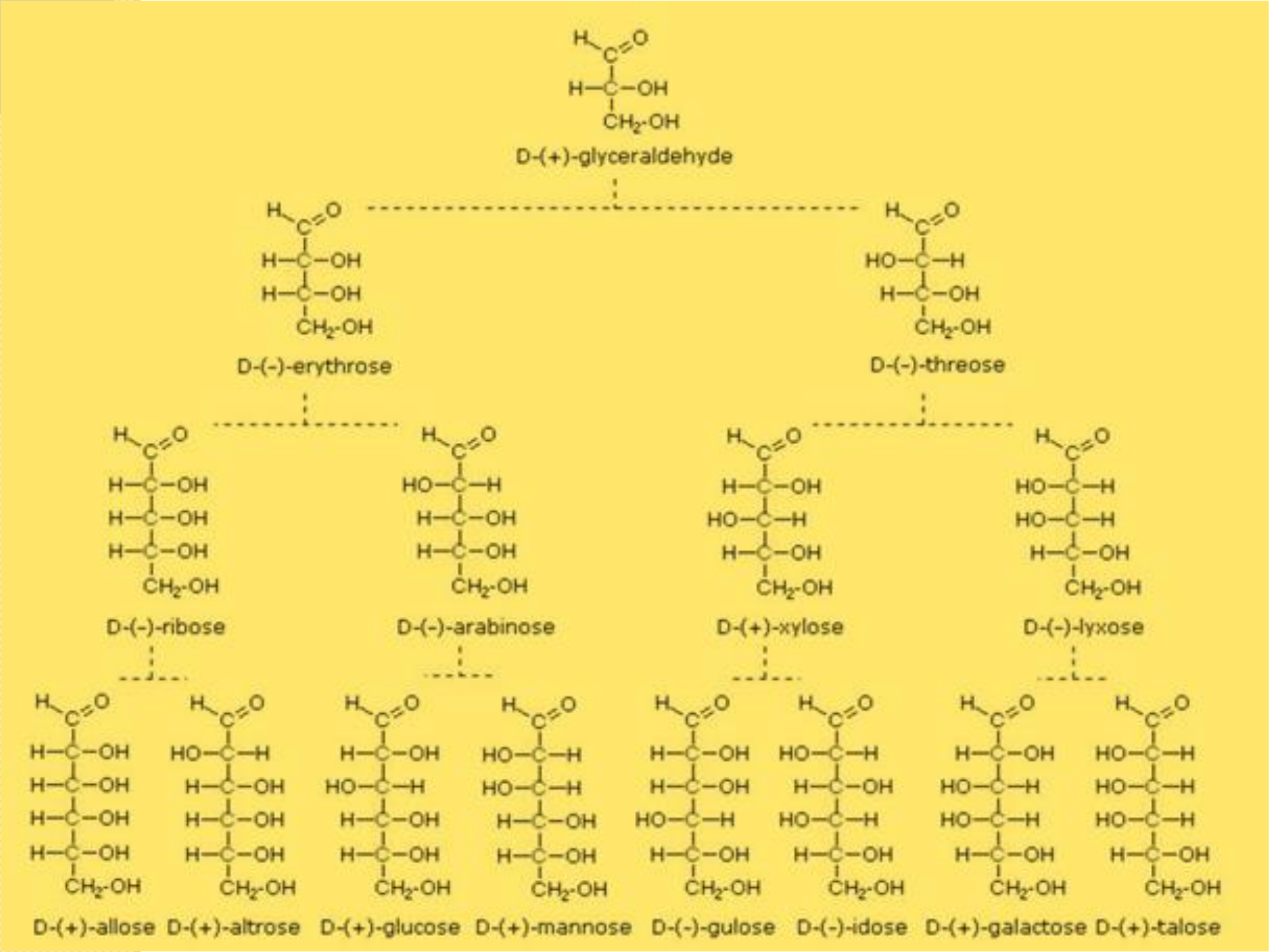


L-glucose

Nomenclature and Structure cont.

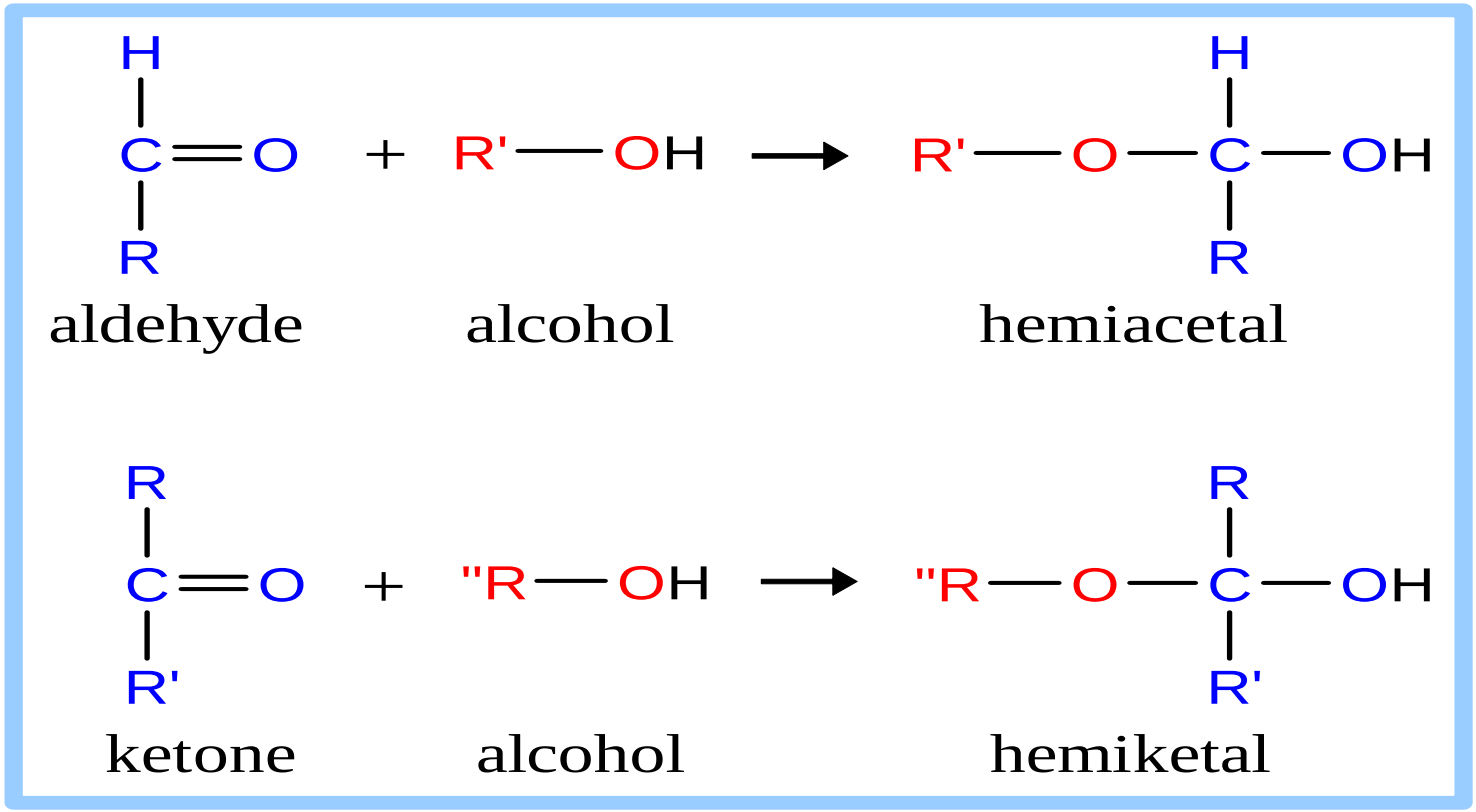
Erythro and Threo

- Terms used for diastereomers with two adjacent chiral C's, without symmetric ends.
- For symmetric molecules, use meso or *d,l*.


D-(+)-glyceraldehyde
D-(-)-erythrose
D-(-)-threose
D-(-)-ribose
D-(-)-arabinose
D-(+)-xylose
D-(-)-lyxose
D-(+)-allose
D-(+)-altrose
D-(+)-glucose
D-(+)-mannose
D-(-)-gulose
D-(-)-idose
D-(+)-galactose
D-(+)-talose

3. Cyclic Structure

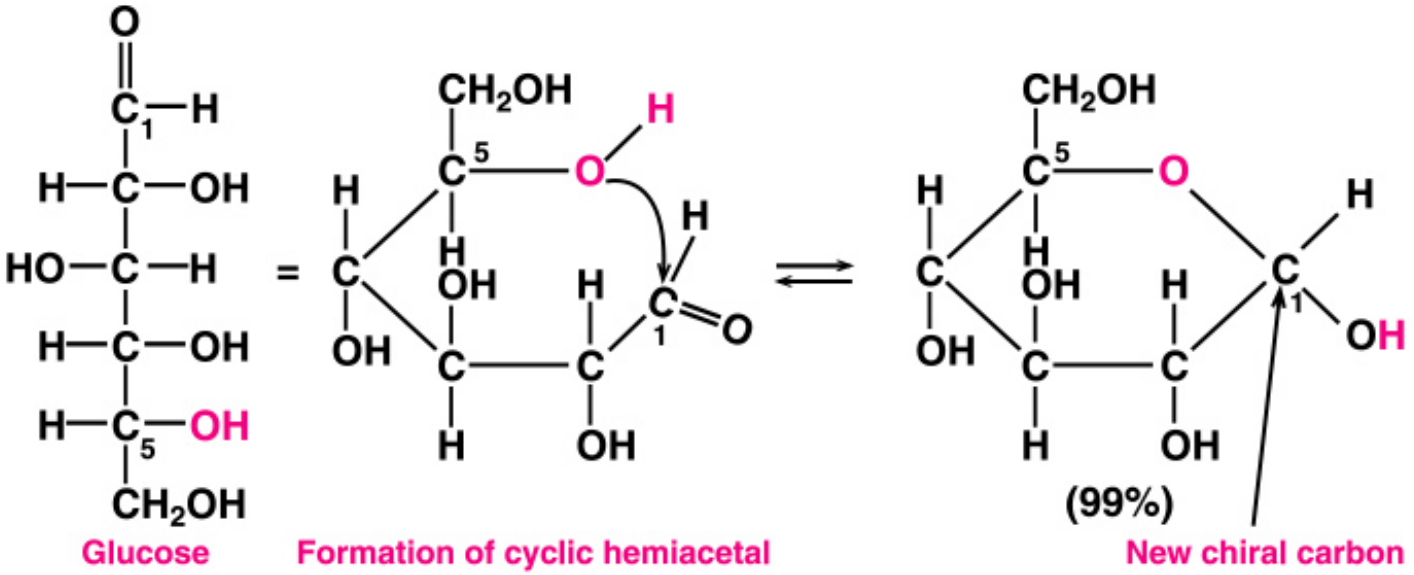
- Hemiacetal & hemiketal formation



Intermolecular hemiacetal and hemiketal formation

Cyclic Structure

- Monosaccharides have, in the same molecule,
  - hydroxyl and
  - carbonyl groups
  - Undergo intra-molecular hemiacetal formation



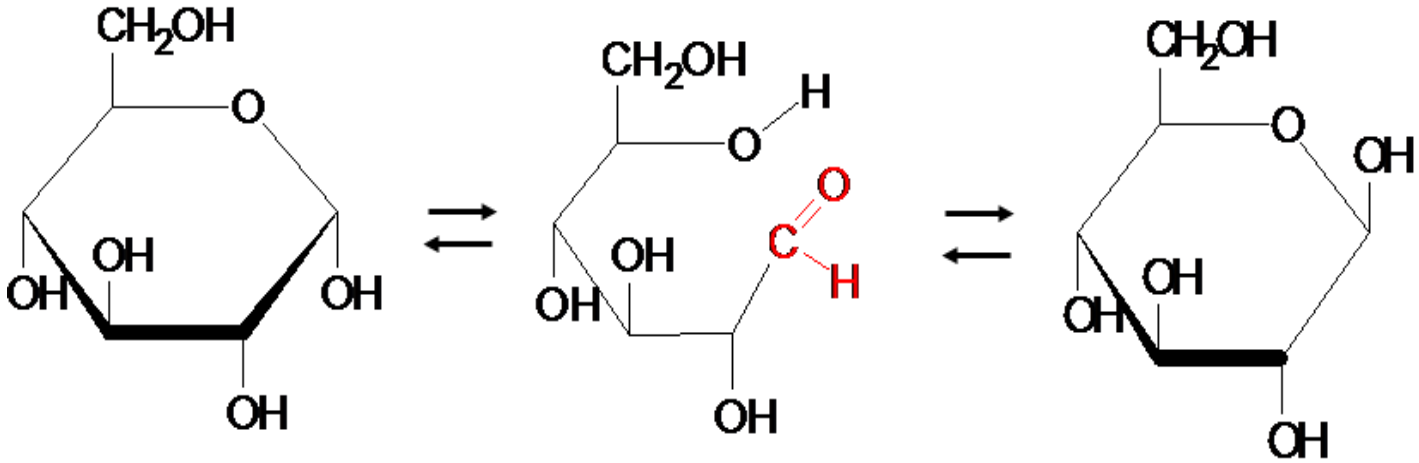
Summary of the Formation of Cyclic Glucose

Cyclic Structure

- α-D-Glucose and β-D-Glucose in Solution

When placed in solution, cyclic structures open and close.

- α-D-glucose converts to *β*-D-glucose and *vice versa*
- There is only a small amount of open chain.



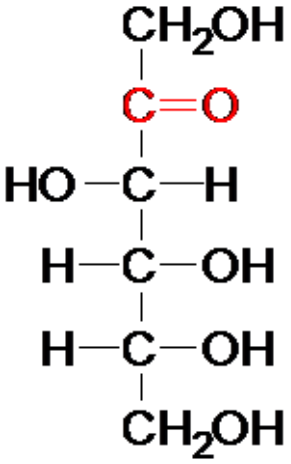
α-D-glucose (36%) ⇌ D-glucose (open) (trace) ⇌ β-D-glucose (64%)

Cyclic Structure

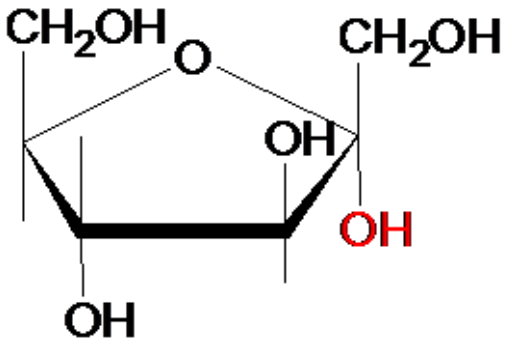
- Cyclic Structure of Fructose

  Fructose

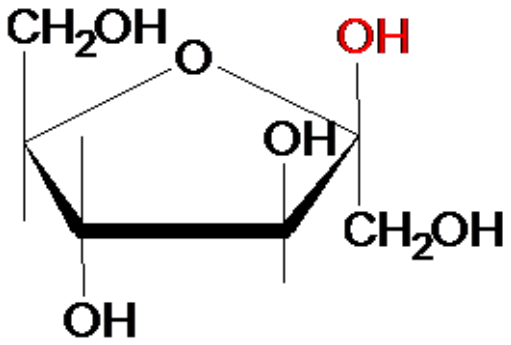
  - Is a ketohexose.
  - Forms a cyclic structure.
  - Reacts the –OH on C-5 with the C=O on C-2.



D-fructose



α-D-fructose

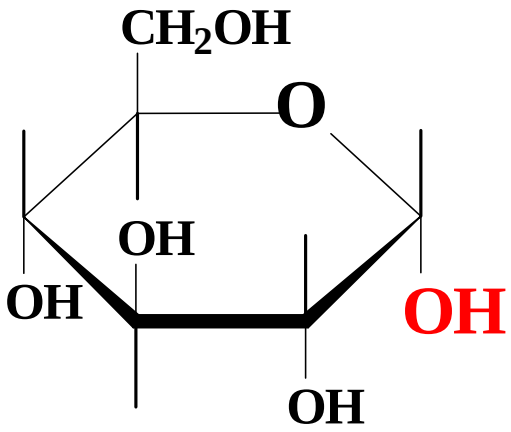


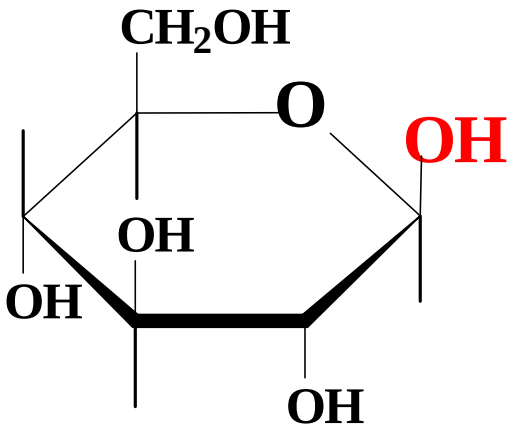
β-D-fructose

- Because monosaccharides form intramolecular hemiacetals,
  - those with five or more carbons exist almost entirely as five- and six-membered cyclic hemiacetals
  - Cyclization produces a new asymmetric center
- **Anomeric carbon:**
  - The new stereocenter created as a result of cyclic hemiacetal formation.
- **Anomers:**
  - Carbohydrates that differ in configuration at their anomeric carbons
  - named α & β anomers
    - α (OH below the ring), β (OH above the ring)

Haworth Projections

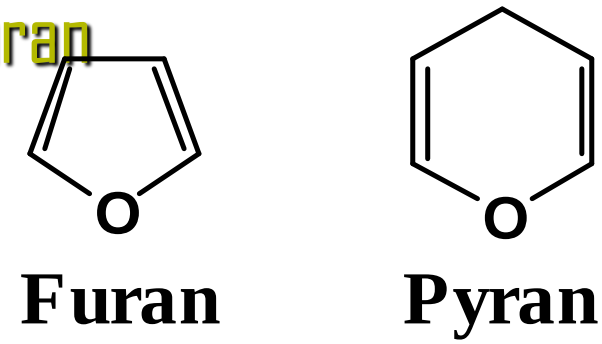
- Haworth projections
  - Five- and six-membered hemiacetals are represented as planar pentagons or hexagons viewed through the edge.
  - They are commonly written with the anomeric carbon on the right and the hemiacetal oxygen to the back right.





Haworth Projections

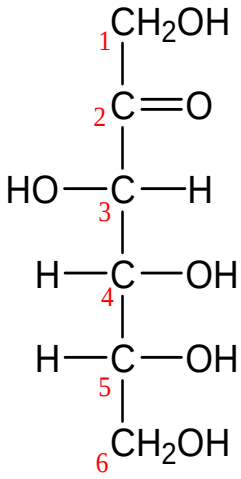
- Six-membered hemiacetal rings are shown by the infix -pyran
- Five-membered hemiacetal rings are shown by the infix -furan



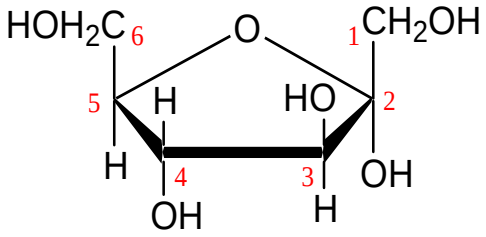
Furan **Pyran**

Haworth Projections

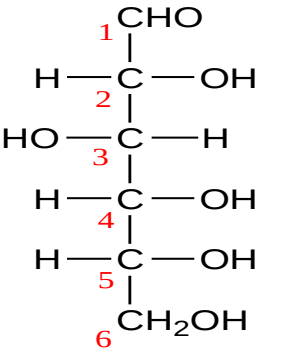
- In haworth projections, use the "right down" and "left up" notion to assign α or β for the hydroxyl groups other than the anomeric hydroxyl group



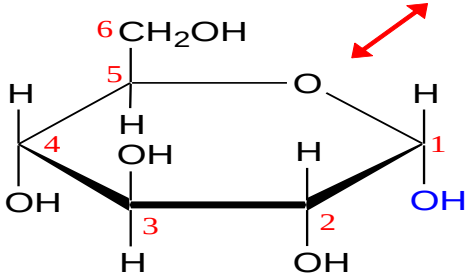
D-fructose (linear)



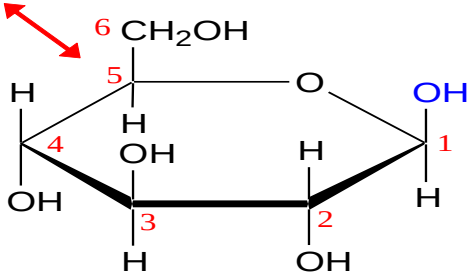
α-D-fructofuranose



D-glucose (linear form)



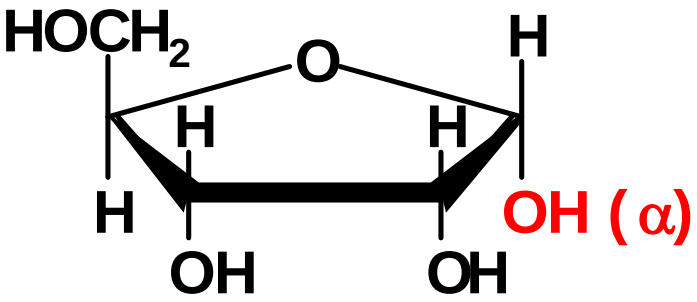
α-D-glucose



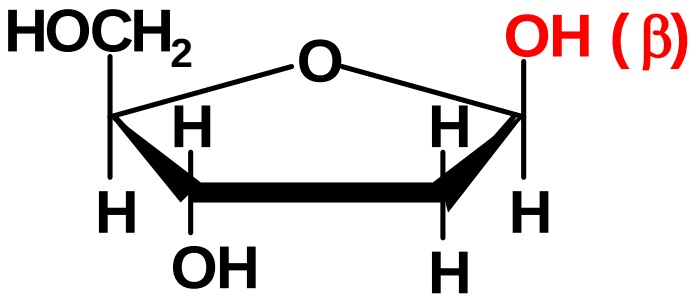
β-D-glucose

Conformational Formulas

- Five-membered rings are so close to being planar that Haworth projections are adequate to represent furanoses.



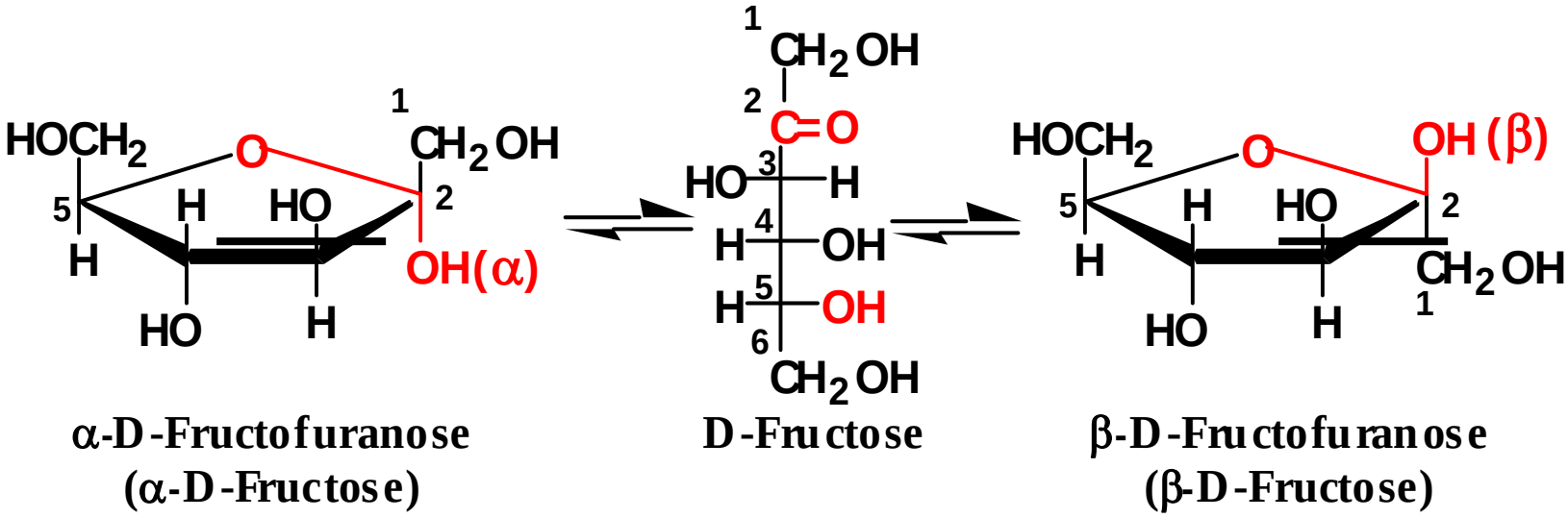
α-D-Ribofuranose
(α-D-Ribose)



β-2-Deoxy-D-ribofuranose
(β-2-Deoxy-D-ribose)

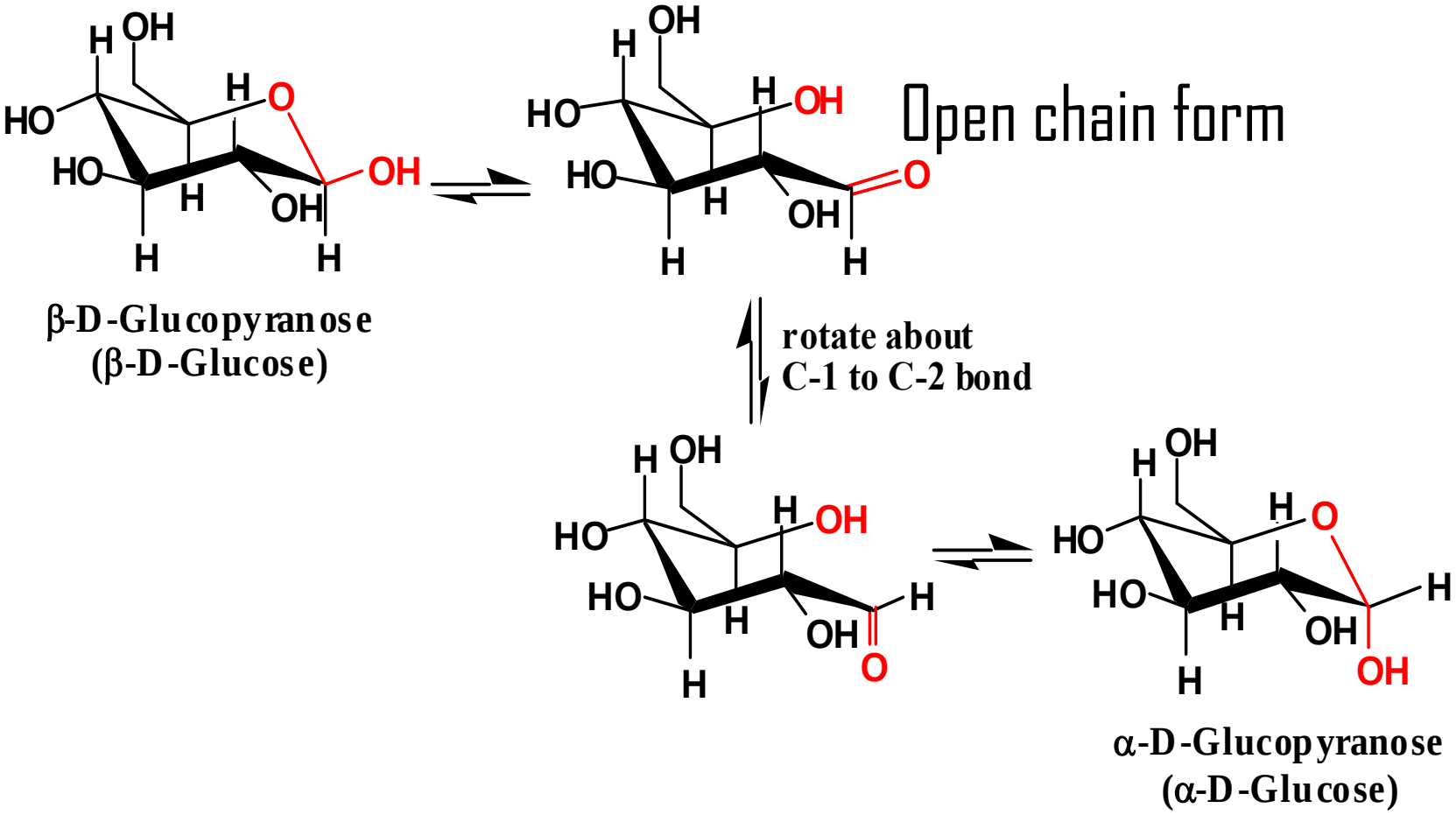
Conformational Formulas

- Other monosaccharides also form five-membered cyclic hemiacetals.
- Here are the five-membered cyclic hemiacetals of D-fructose, a ketohexose.



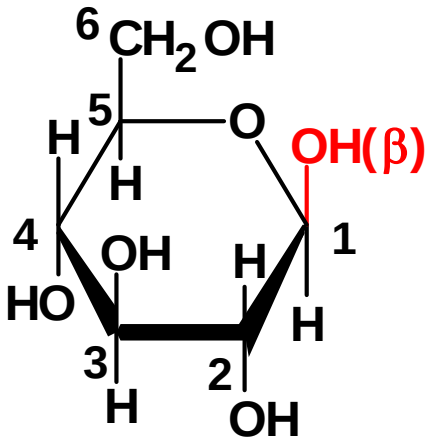
Conformational Formulas; β to α conversion

- For pyranoses, the six-membered ring is more accurately represented as a chair conformation.

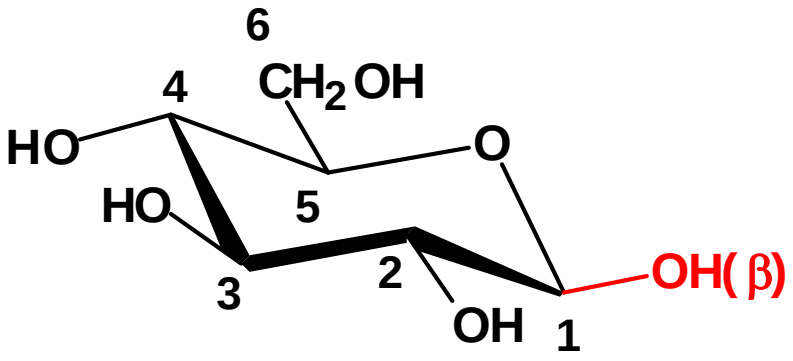


Conformational Formulas

- The orientations of groups on carbons 1-5 in the Haworth and chair projections of β-D-glucopyranose are up-down-up-down-up.



β-D-Glucopyranose
(Haworth projection)

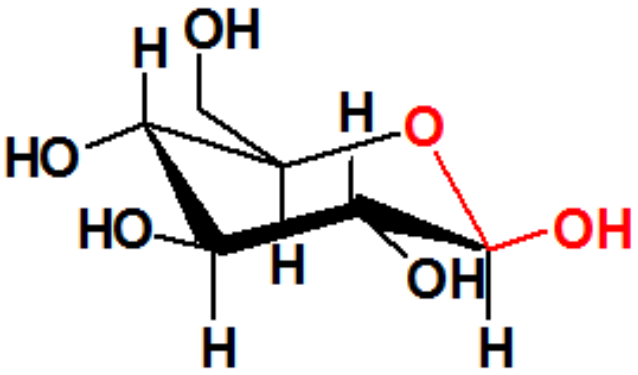


β-D-Glucopyranose
(chair conformation)

Mutarotation

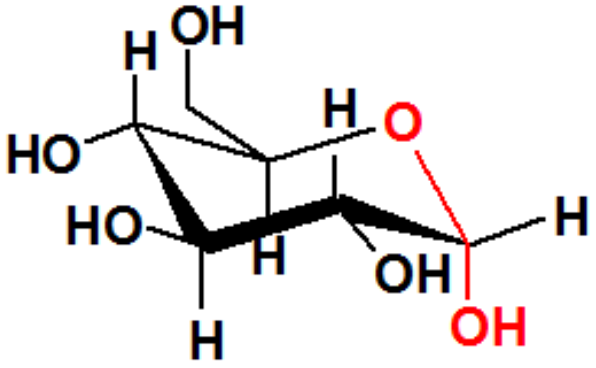
- Mutarotation
  - ➢ is a term given to the change in the observed optical rotation of a substance with time.
- For example, glucose
  - ➢ can be obtained in either its α or β-pyranose form.
  - ➢ The two forms have different physical properties such as melting point and optical rotation.
- When either form is dissolved in water,
  - ➢ its initial rotation changes with time.
- Eventually both solutions have the same rotation.

Mutarotation of D-Glucose



β-D-Glucopyranose
(β-D-Glucose)

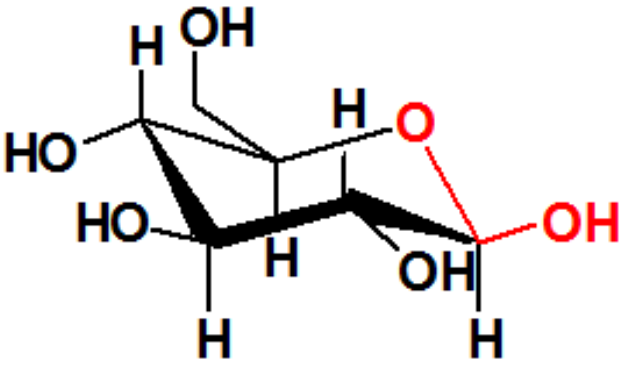
Initial: $[\alpha]_D$ +18.7°



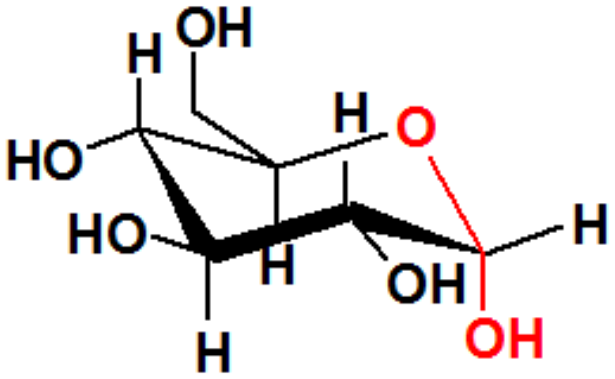
α-D-Glucopyranose
(α-D-Glucose)

Initial: $[\alpha]_D$ +112.2°

Mutarotation of D-Glucose



β-D-Glucopyranose



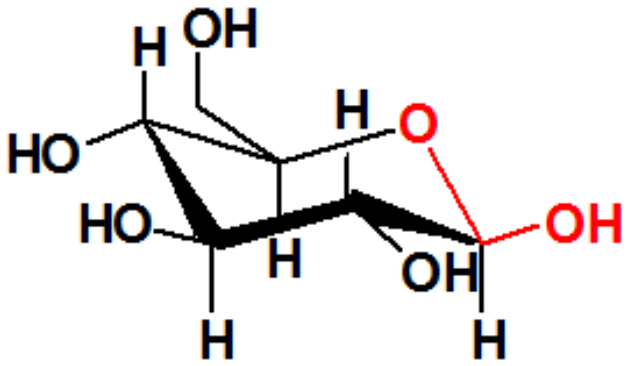
α -D-Glucopyranose

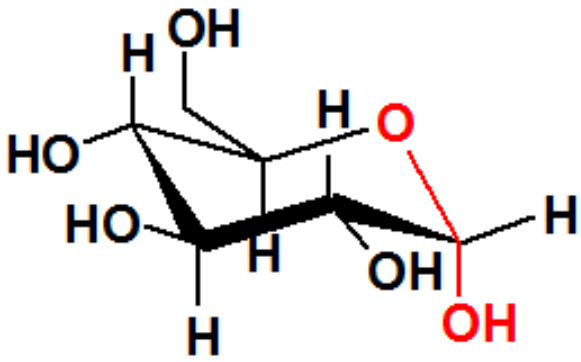
Initial: $[\alpha]_D$ +18.7°

Initial: $[\alpha]_D$ +112.2°

Final: $[\alpha]_D$ +52.5°

Mutarotation of D-Glucose





β-D-Glucopyranose α-D-Glucopyranose

- **Explanation**: After being dissolved in water, the α and β forms slowly interconvert via the open-chain form. An equilibrium state is reached that contains 64% β and 36% α

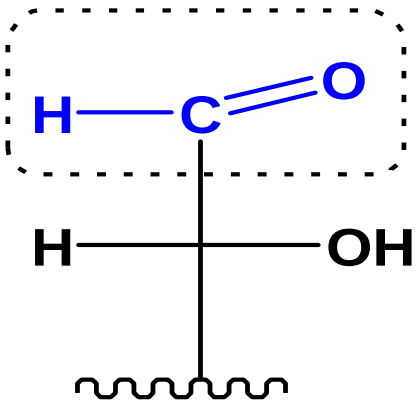
.

4. Reactions of monosaccharides

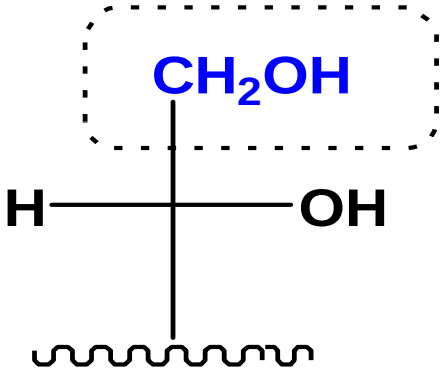
- Carbonyl reactions
  - Reduction
  - Oxidation
  - Chain Shortening and Lengthening
  - Osazone formation
- Peroxidation
- Alcohol reactions
  - Glycoside formation
  - Ether formation
  - Ester formation

4.1 Reduction reactions

- The C=O of aldoses or ketoses can be reduced to C-OH
- Done enzymatically or catalytically by
  - sodium borohydride ($NaBH_4$) or
  - hydrogenation (H_2/Ni).
- the resultant product is a polyol or sugar alcohol (**alditol**)
- The formed sugar alcohol is named by adding **-itol** to the root name of the sugar

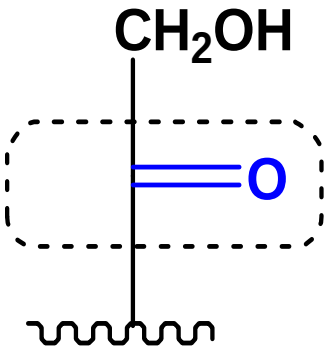


$NaBH_4 / H_2O$ or H_2/Ni

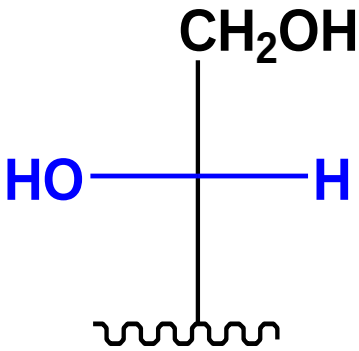


Aldehyde

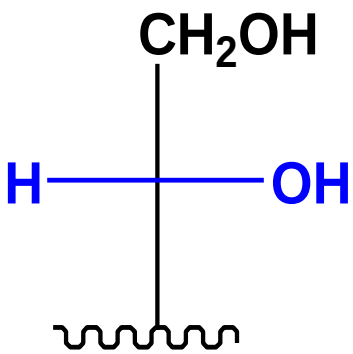
Alcohol



$NaBH_4 / H_2O$ or H_2/Ni



or



Ketone

Alcohols

Reduction

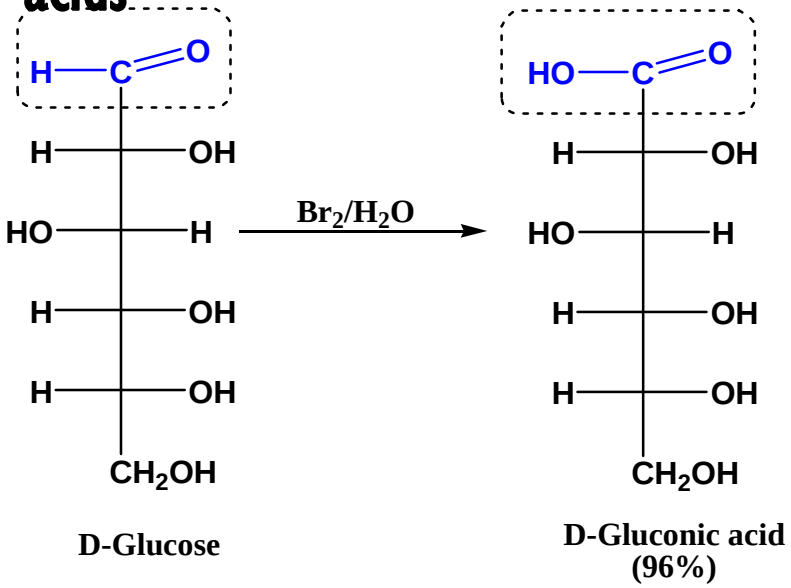
- Examples
  - ✓ glucose form glucitol (sorbitol)
  - ✓ mannose forms mannitol
  - ✓ fructose forms a mixture of mannitol and sorbitol
  - ✓ glyceraldehyde gives glycerol

4.2 Oxidation reactions

- Aldoses may be oxidized to 3 types of acids
  - Aldonic acids
  - Uronic acids
  - Aldaric acids

i. Mild Oxidation by Bromine

- **Aldonic acids**:
  - ✓ Aldehyde group is converted to a carboxyl group
  - ✓ Example: glucose – gluconic acid)
- Bromine water
  - oxidizes aldehyde, but not ketone or alcohol; and
  - forms **aldonic acids**



D-Glucose

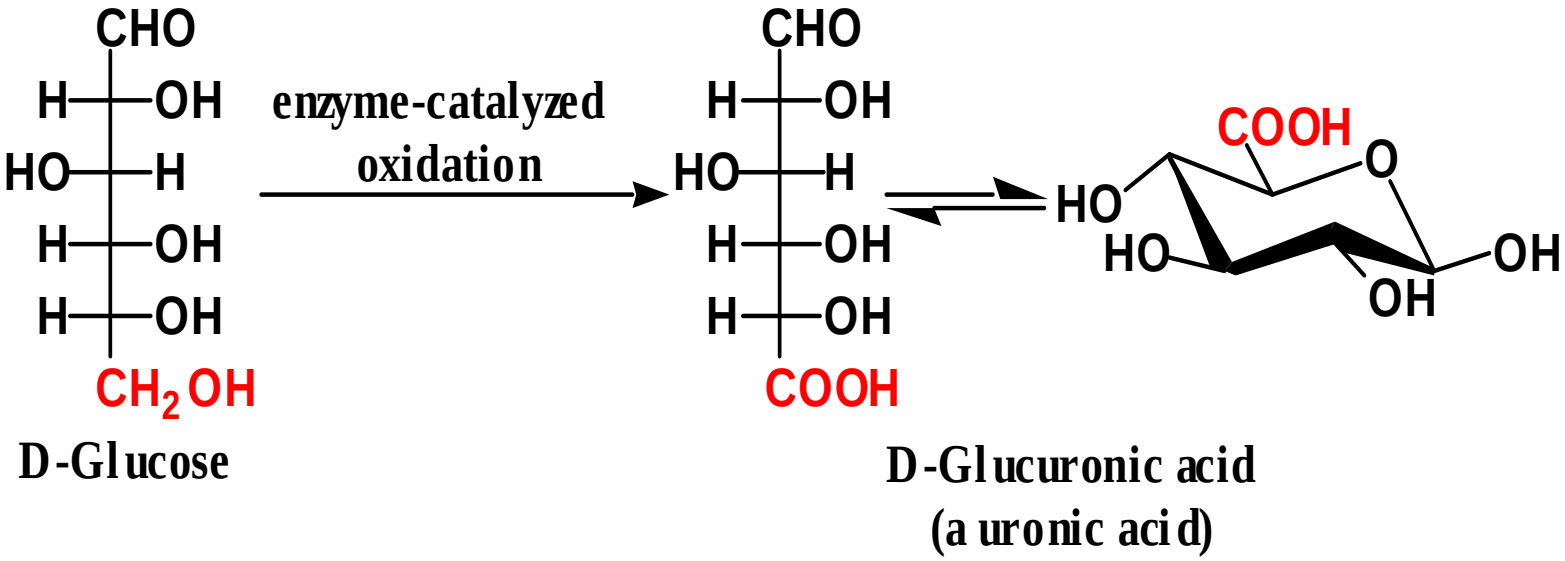
D-Gluconic acid (96%)

Mild Oxidation. Cont.

- Other reagents used for mild oxidation include:
  - Cu^{++} (Fehling's or Benedict's test) and
  - Ag^{+} (Tollen's test) are also used;
- but these are less important because:
  - they cannot differentiate aldoses from ketoses(the base promotes enediol rearrangements, so ketoses react too) and hence
  - not used to prepare aldonic acids from aldose

Oxidation reactions

- **Uronic acids**:
  - aldehyde is left intact and primary alcohol at the other end is oxidized to COOH
  - Example: Glucose --- glucuronic acid; Galactose --- galacturonic acid



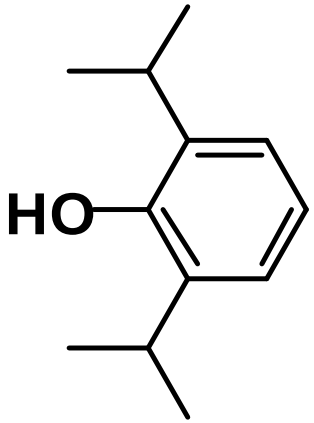
D-Glucose

D-Glucuronic acid
(a uronic acid)

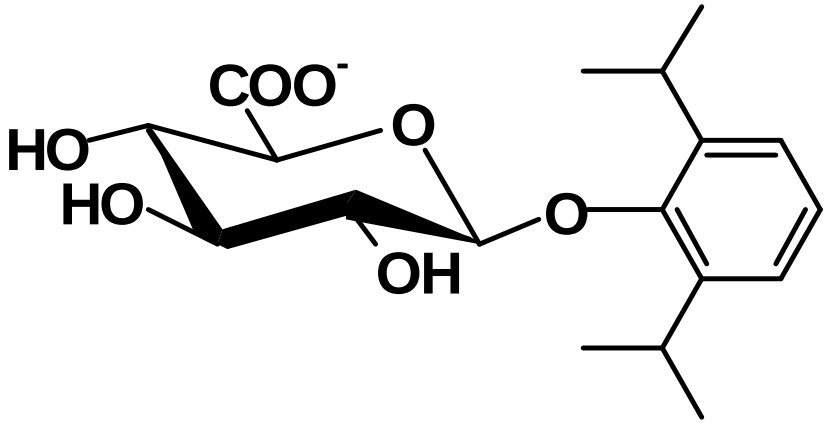
Uronic acids Cont.

- In humans, D-gluconic acid is
  - an important component of the acidic polysaccharides of connective tissue.
- It is also used by the body to detoxify foreign hydroxyl-containing compounds, such as phenols and alcohols;
  - one example is the intravenous anesthetic propofol.

Reactions of monosacch. Cont.



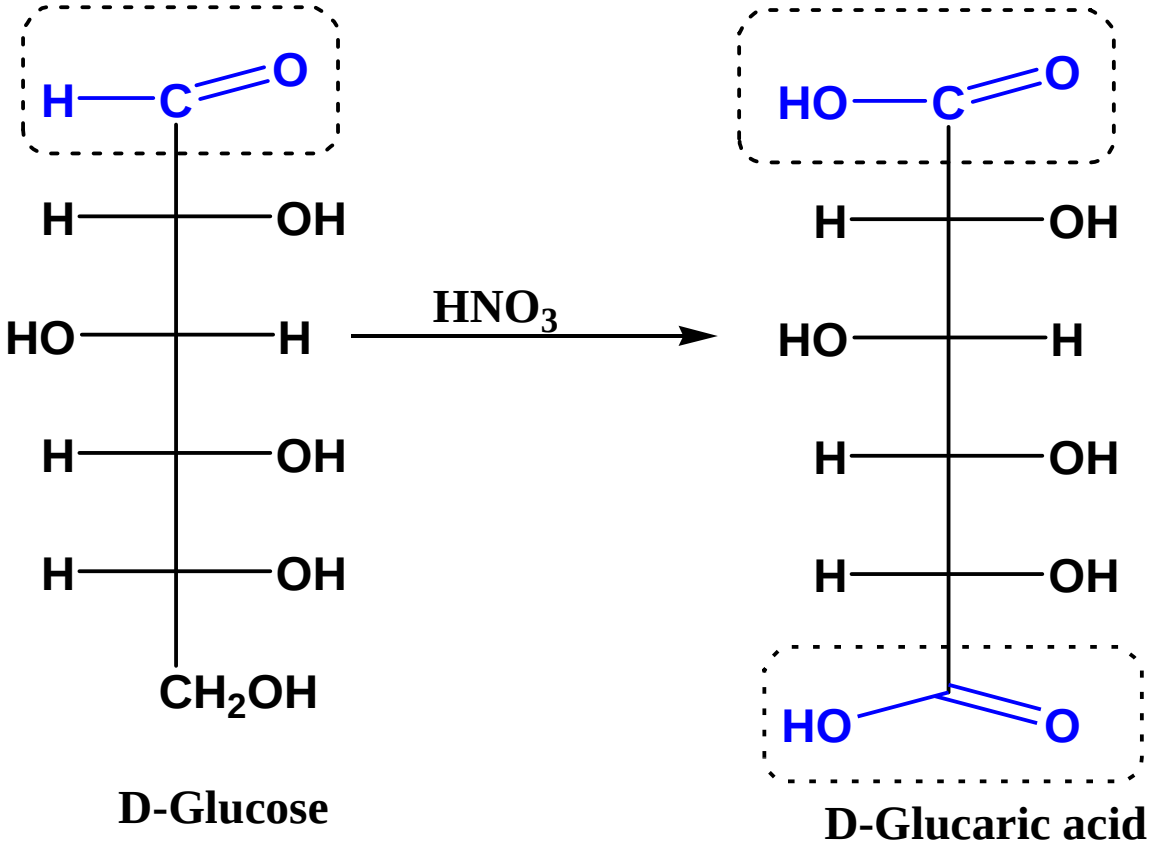
Propofol



A urine-soluble glucuronide

ii. Strong Oxidation by Nitric Acid

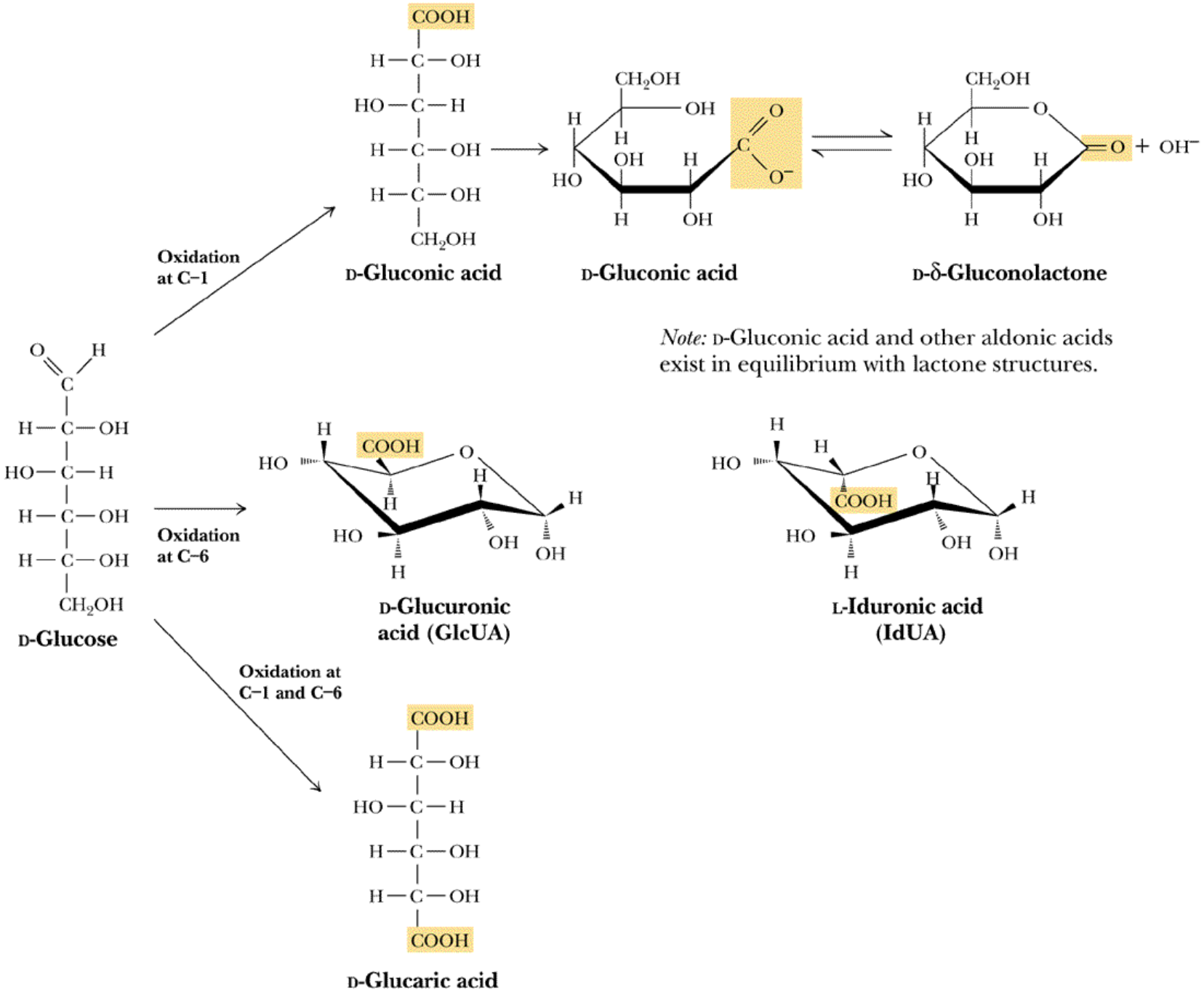
- **Aldaric acids**
  - Also called Saccharic acids (glycaric acids)
  - oxidation at both ends of monosaccharide
  - Example:
    - Glucose ---- Glucaric acid
    - Galactose --- Galactaric acid
    - Mannose --- mannaric acid
  - Nitric acid
    - Oxidizes both the aldehyde and the terminal alcohol and
    - generates an aldaric acid.



D-Glucose **D-Glucaric acid**

Reactions of monosacch. Cont.

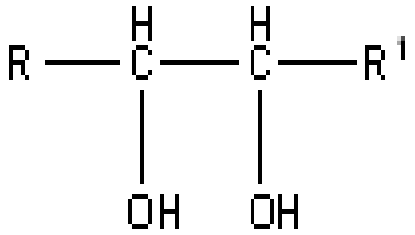
- Important to reduce the number of chiral centers
- For example, if a D- aldohexose is oxidized to give a meso aldaric acid, then the original hexose sugar has
  - either all the OH groups on the same side or
  - its OH groups must be arranged in such away that these in (C-2 & C-5) and (C-3 & C-4) are mirror image of one another.


COOH
CH2OH
D-Gluconic acid
D-Gluconic acid
D-δ-Gluconolactone
+ OH−
Oxidation at C−1
Note: D-Gluconic acid and other aldonic acids exist in equilibrium with lactone structures.
D-Glucose
Oxidation at C−6
D-Glucuronic acid (GlcUA)
L-Iduronic acid (IdUA)
Oxidation at C−1 and C−6
D-Glucaric acid

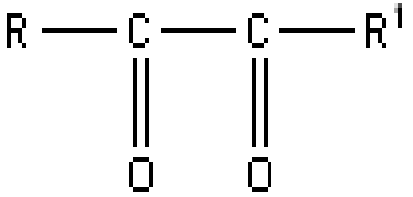
iii. Per oxidation (Periodic Acid Cleavage)

- **Periodic acid (HIO_4)**
  - Cleaves cpds that contain two or more C–OH or C=O groups on adjacent carbon atoms,
    - Carbohydrates are one such cpds
  - Cleaves vicinal diols to give two carbonyl compounds.
  - Separation and identification of the products determine the size of a ring.

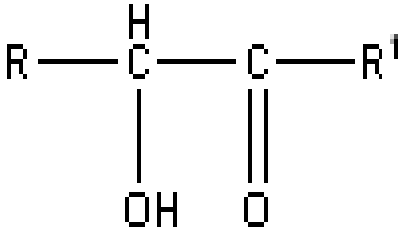
Periodic Acid Cleavage Cont.



+ HIO_4 ⟶ RCHO + R^1CHO

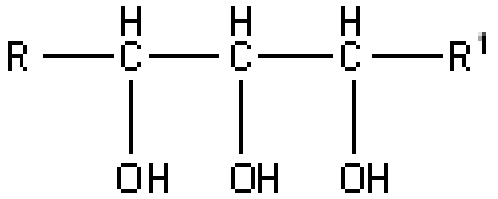


+ HIO_4 ⟶ RCOOH + R^1COOH

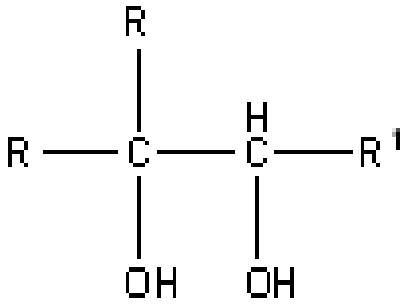


+ HIO_4 ⟶ RCHO + R^1COOH

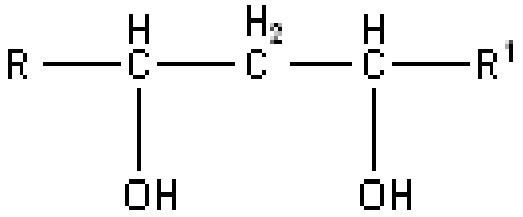
Periodic Acid Cleavage Cont.



+ HIO_4 ⟶ RCHO + HCOOH + R^1CHO



+ HIO_4 ⟶ R_2CO + R^1CHO



+ HIO_4 ⟶ No reaction

4.3 Methods of Lengthening and Shortening Chains

Cyanohydrin formation-chain lengthening

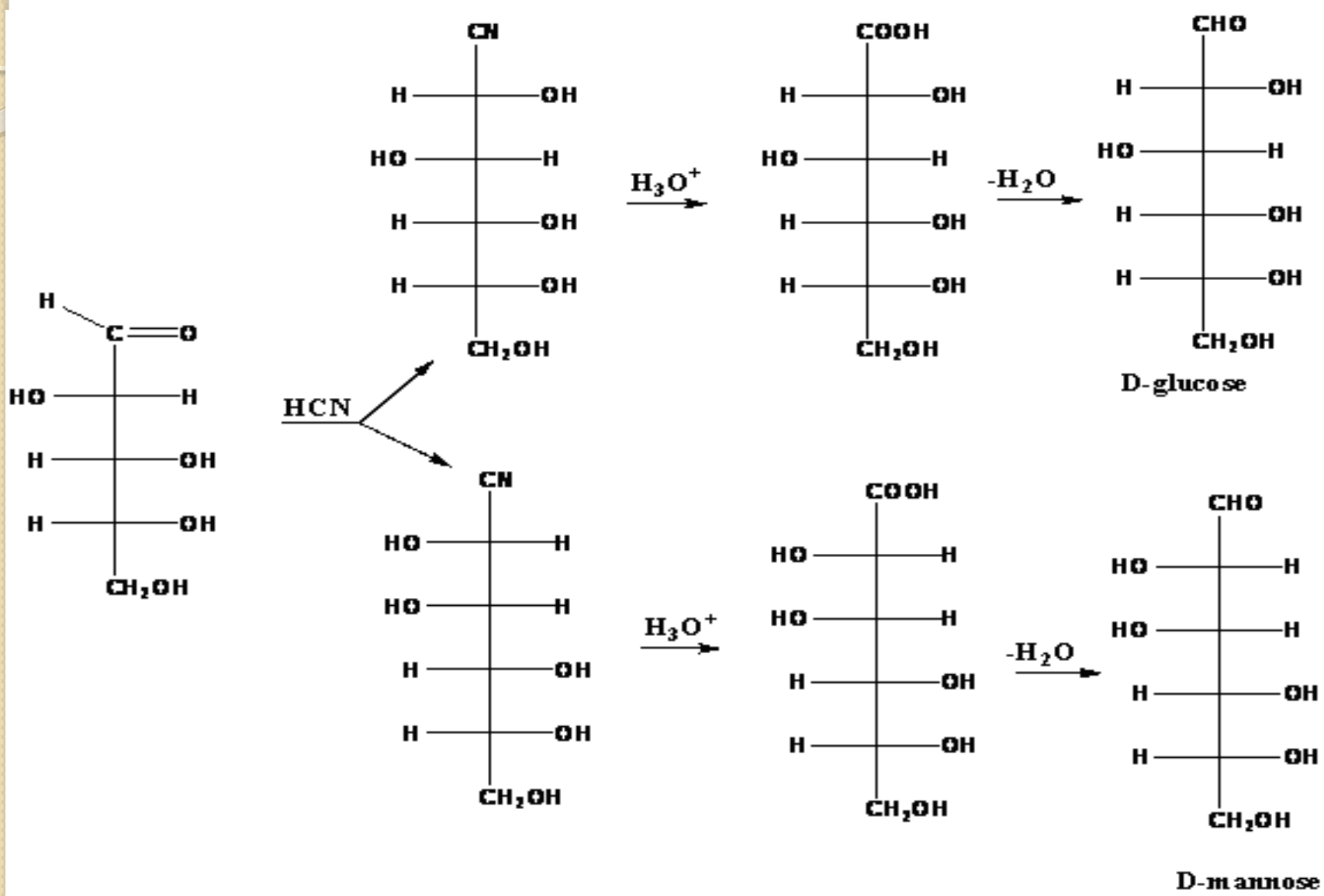
- Reaction of an aldose with HCN
- Used to ↑ chain length of monosaccharides
- Results in a cyanohydrin which is then hydrolyzed to an acid and reduced to the aldehyde
- Can prepare all monosaccharides from D-glyceraldehyde
- Known as the Fischer-Kiliani synthesis

Kiliani-Fischer Synthesis

- Generates two sugars, each longer than the starting sugar by one C.
  - A mixture of C-2 epimers is formed
- Can be used not only to synthesize new carbohydrates but also helps to determine their configuration.

Reactions of monosacch. Cont.

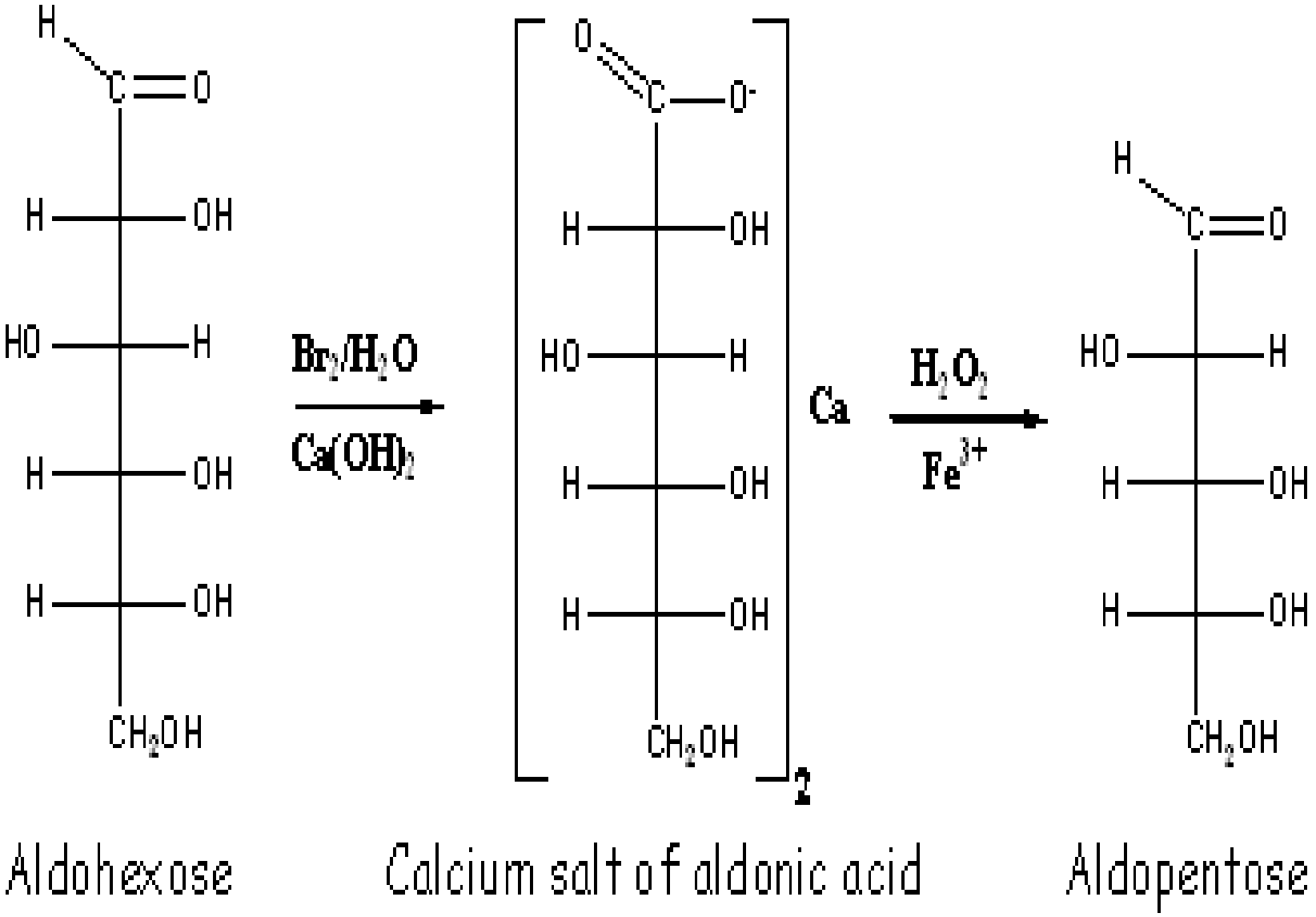
✓Example of Kiliani-Fischer synthesis chain lengthening



The Ruff degradation-chain shortening

- The Ruff degradation
  - shortens the starting sugar by one carbon
  - It is the original aldehyde carbon that is lost!
  - Mechanism complicated!
  - An example of net reaction is given below

✓Example of the Ruff degradation chain shortening

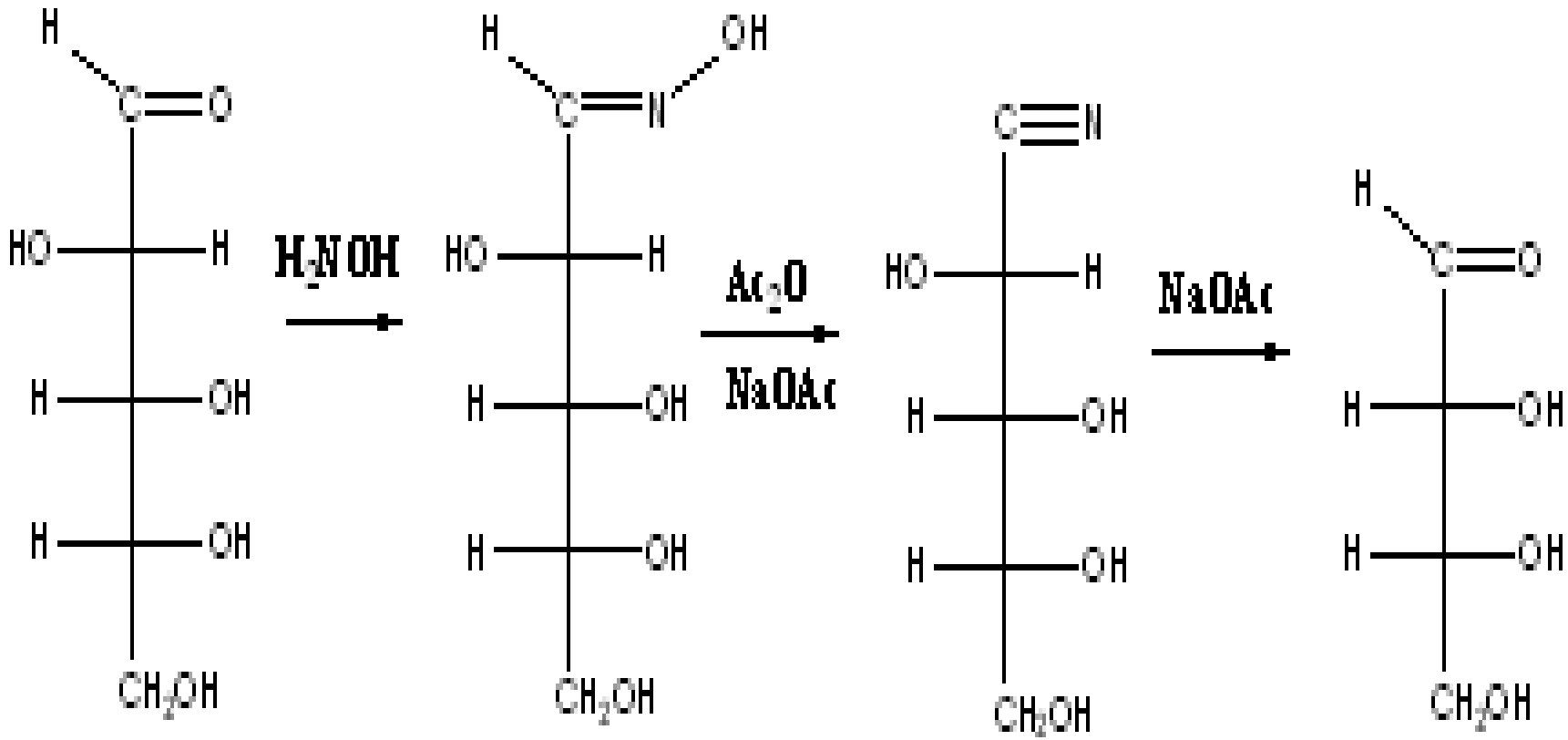


The Wohl degradation

- Also shortens sugars by loss of the aldehyde carbon.
- Gives better degradation for pentose sugars than the Ruff degradation
- Involve amine oxide, acetic anhydride and sodium acetate

Reactions of monosacch. Cont.

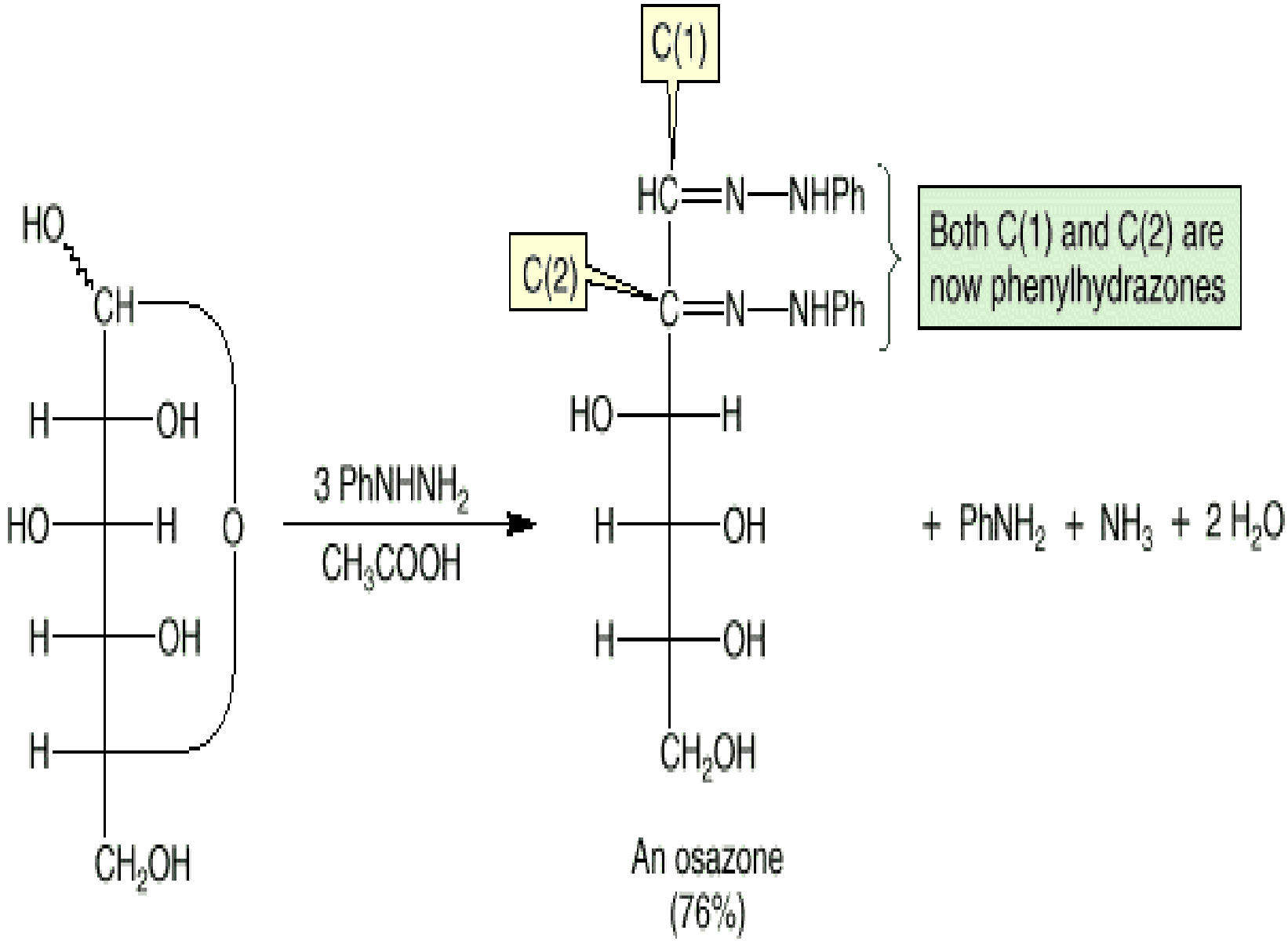
✓Example of The Wohl degradation chain shortening



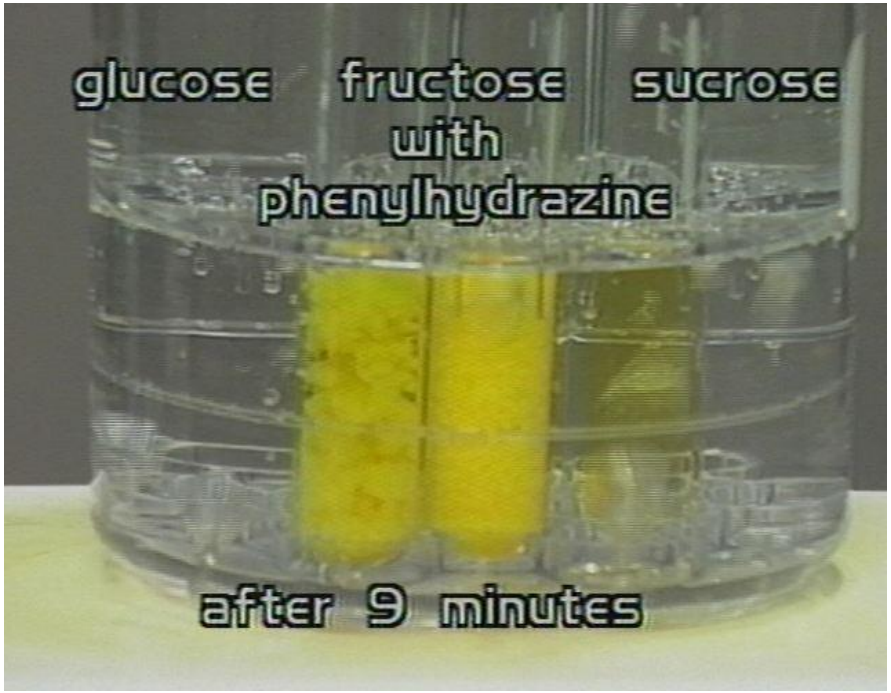
Aldopentose oxime

4.4 Osazone Formation

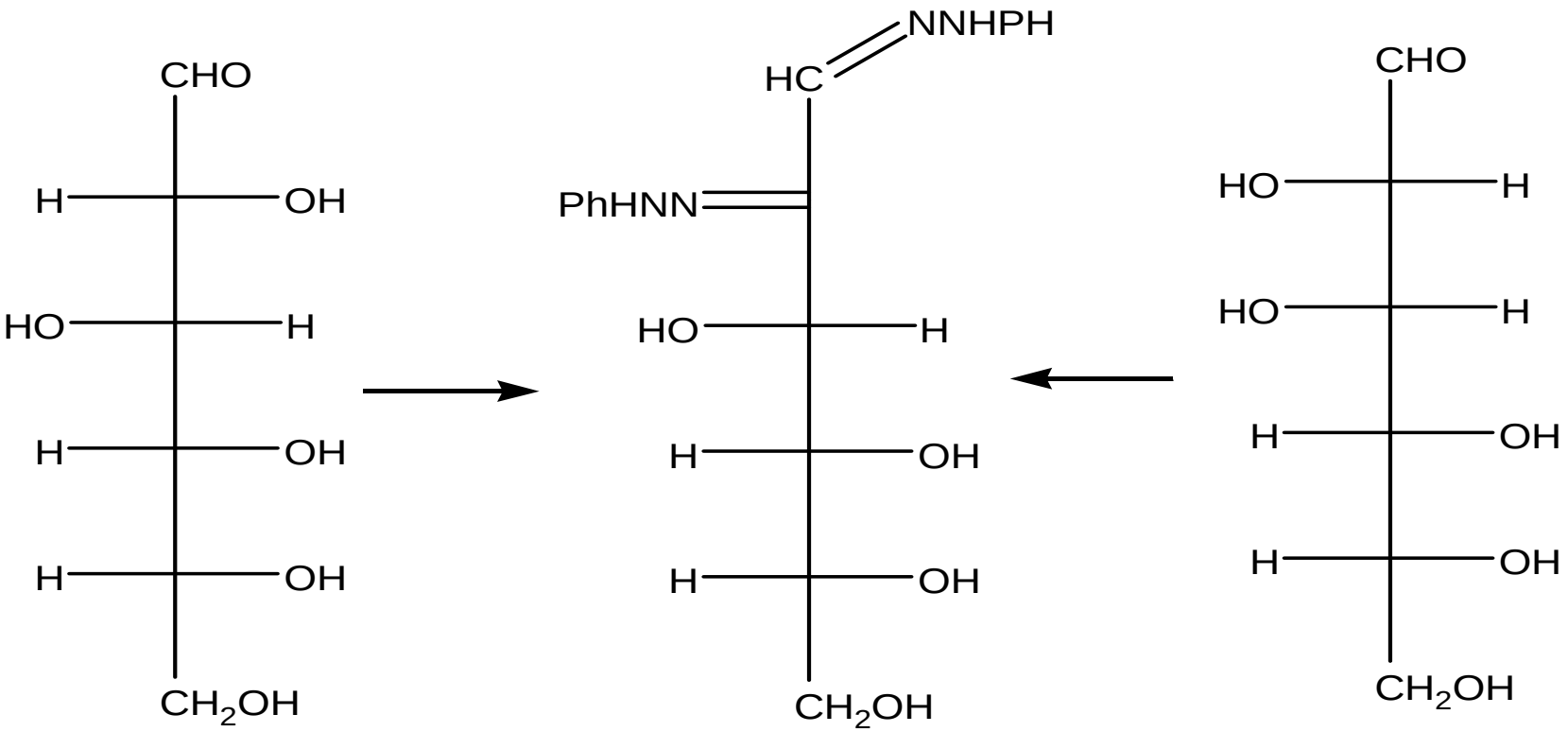
- Both C-1 and C-2 react with phenylhydrazine.
- Treatment of carbohydrates with phenylhydrazine (C_6H_5-$NHNH_2$) leads to phenylhydrazone formation with the carbonyl.
- Treatment with 3 equiv. of phenyl-hydrazine leads to osazone formation.


C(1)
C(2)
HC=N—NHPh
C=N—NHPh
Both C(1) and C(2) are now phenylhydrazones
HO
CH
H—OH
HO—H
O
H—OH
H
CH2OH
3 PhNHNH2
CH3COOH
HO—H
H—OH
H—OH
CH2OH
An osazone
(76%)
+ PhNH2 + NH3 + 2 H2O

- The formed osazone is a crystalline cpd with a sharp mp
- Once used for the identification of sugars
- Seldom used for identification; we now use HPLC or mass spectrometry



- **D-glucose, D-fructose and D-mannose give the same osazone**

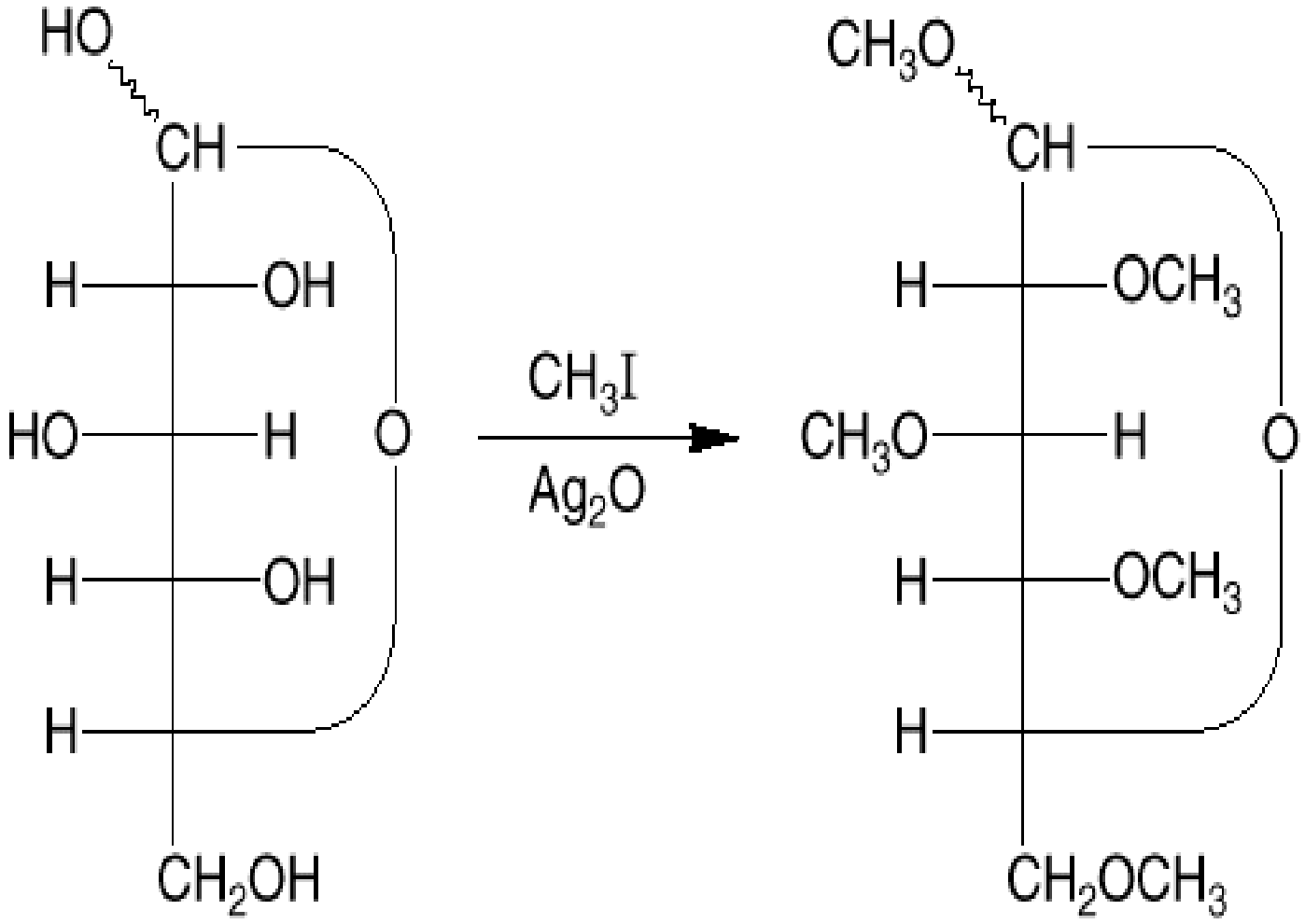


D glucose

D mannose

Ether formation

- Treatment of a sugar with methyl iodide and silver oxide leads to methylation at every free hydroxyl group in the molecule.
  - Alkoxides can displace halides to make ethers.
  - This reaction is the **Williamson ether synthesis**.

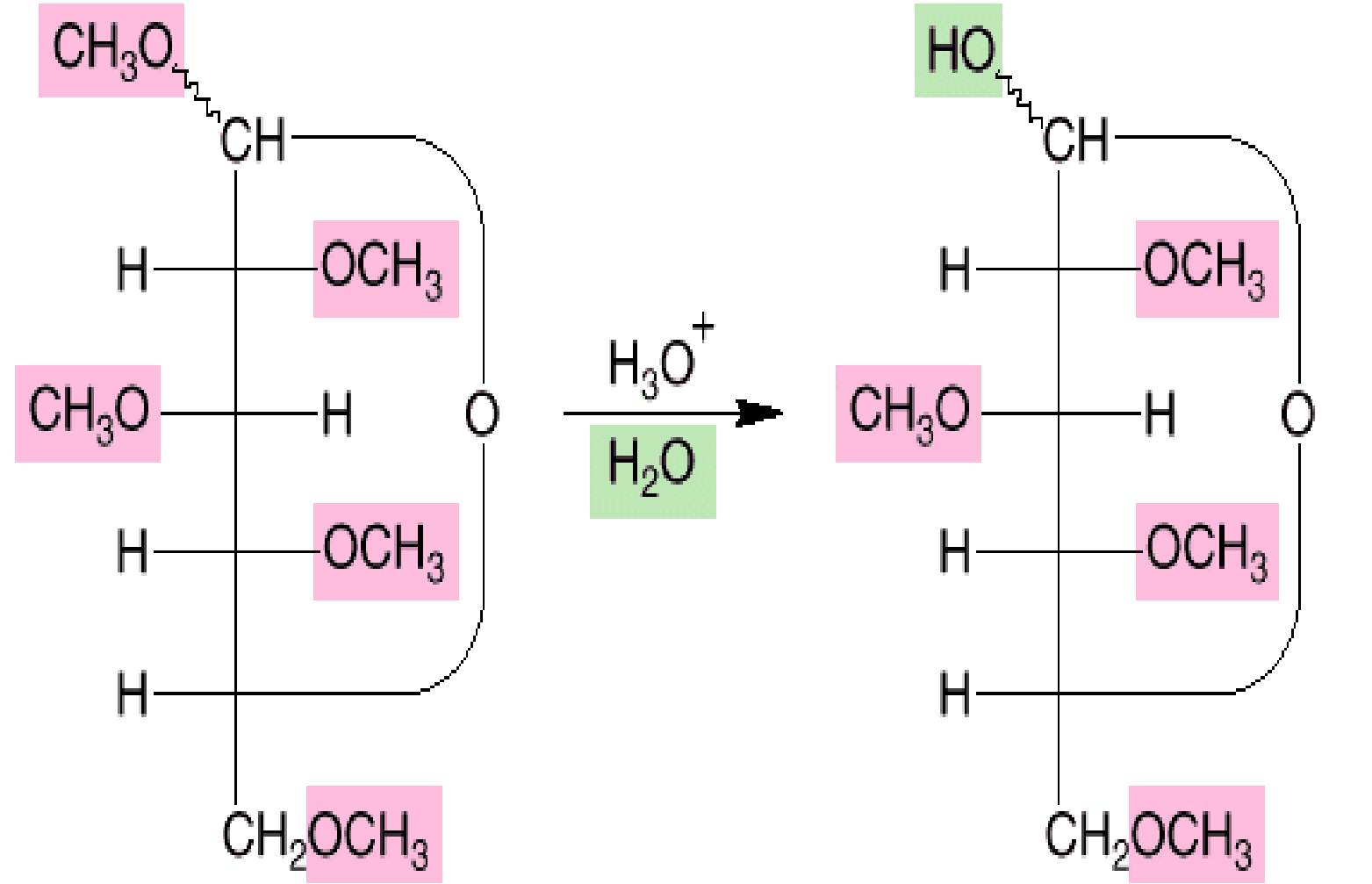


(~ 55%)

D-Glucopyranose **1,2,3,4,6-Pentamethoxy-D-glucose**

- Hydrolysis of the fully methylated compounds leads to a hemiacetal in which only the methoxyl group at the anomeric position (C-1) has been converted into an OH.

Reactions of monosacch. Cont.

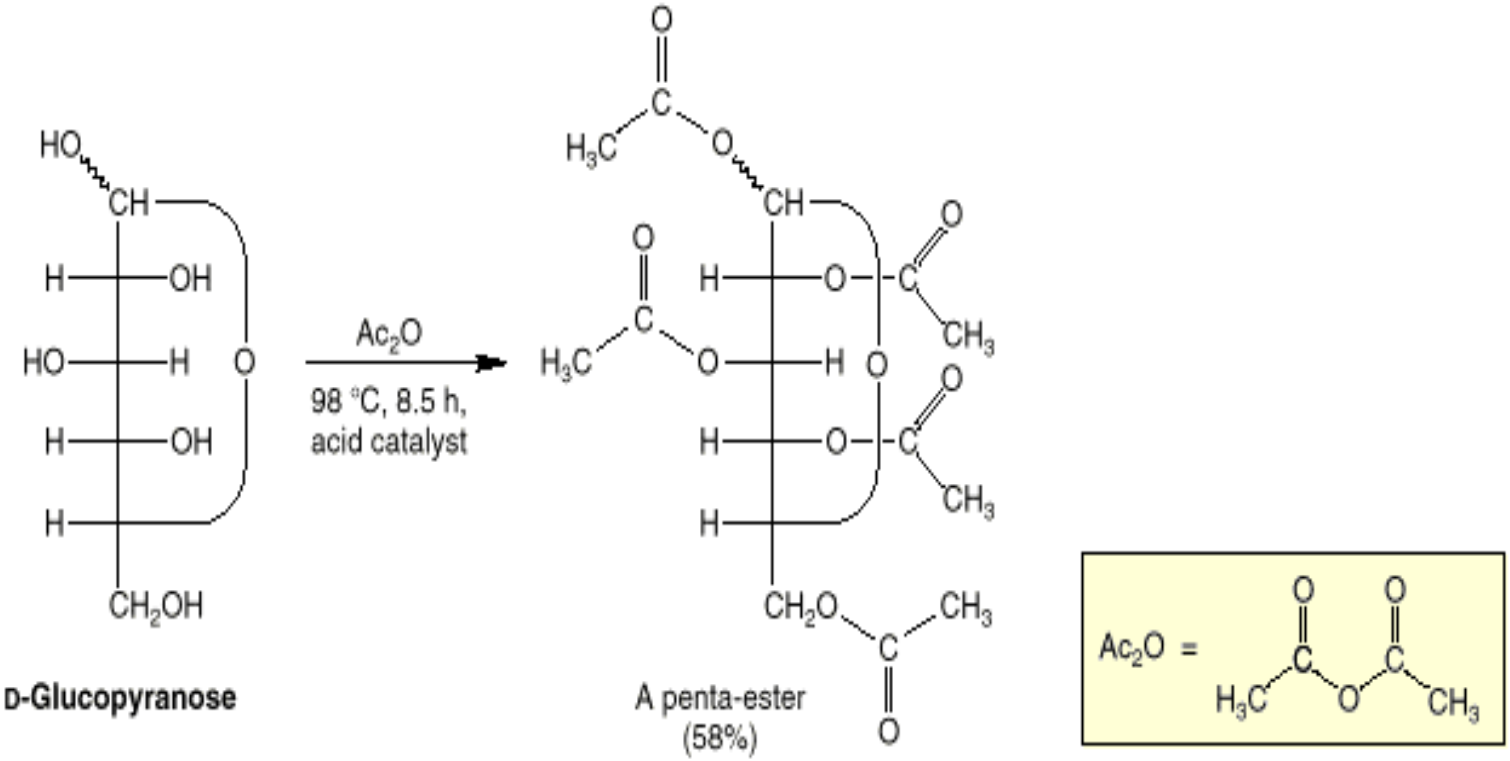


A tetra-ether, monoacetal

A tetra-ether, hemiacetal

4.6 Ester Formation

- All free hydroxyl groups can be esterified with acetic anhydride with pyridine catalyst .



D-Glucopyranose

Determination of ring size

- 6-membered ring of cyclic structures of monosacharides is usually considered
  - But other ring size is possible, eg 5-membered ring
- When methyl-glucoside is treated with methylsulfate and sodium hydroxide, and the product is hydrolyzed by dilute HCl, a tetra-O-mthyl glucose is obtained

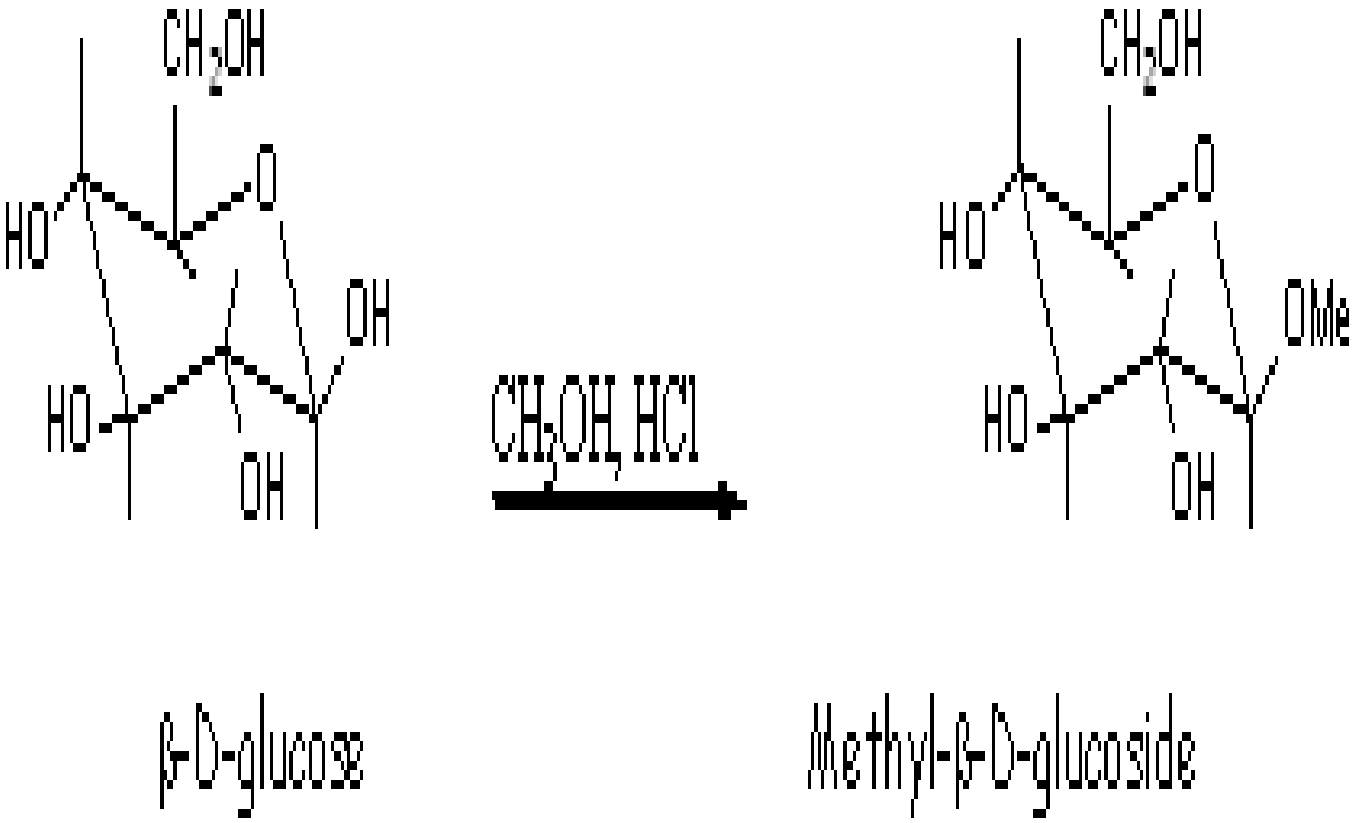
Determination of ring size cont.

- The tetra-O-mthyl glucose is a cyclic hemiacetal, which, in solution, exists in equilibrium with a little of the open chain form
- The open chain tetra-O-mthyl-D- glucose contains an aldehyde group and four $-OCH_3$ groups

Determination of ring size cont.

- It also contains a free, unmethylated –OH group at which ever carbon was originally involved in the acetal ring
  - On C-5 if the six membered ring is correct
  - On C-4 if the five membered ring is correct etc

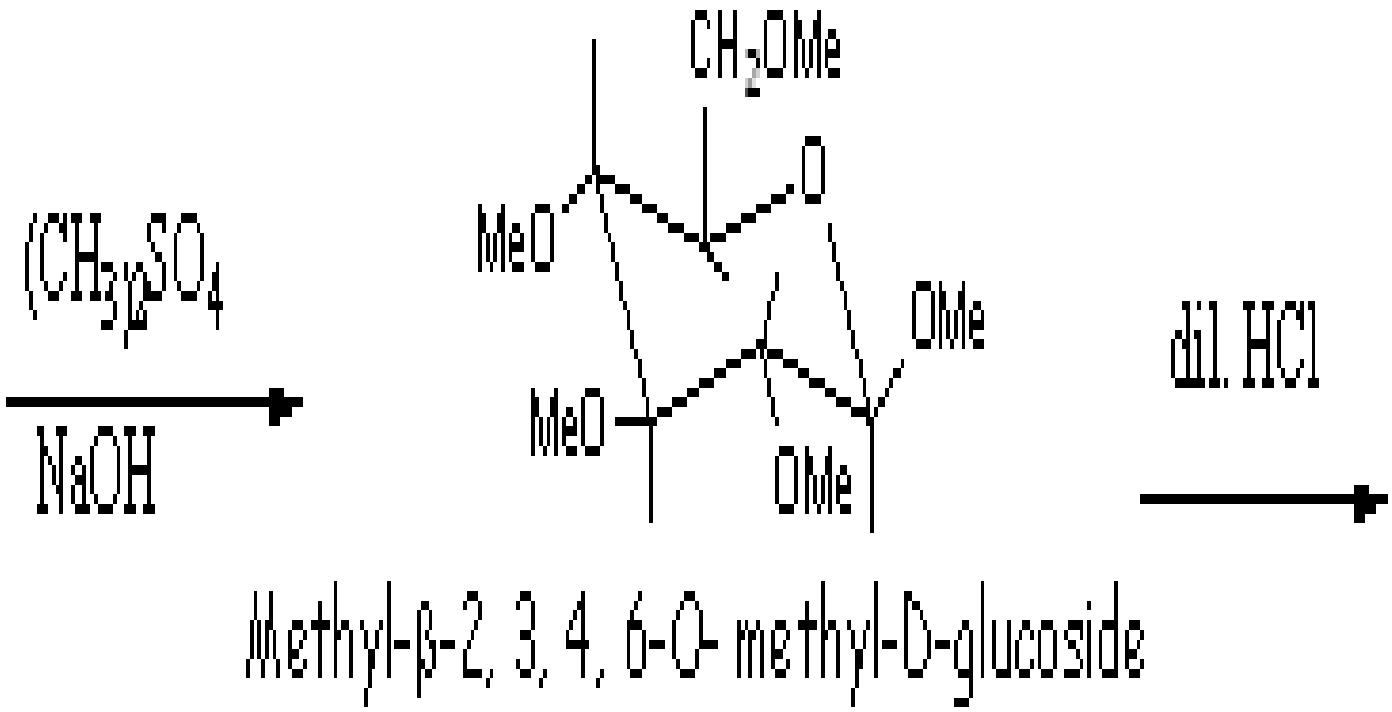
Determination of ring size cont.



β-D-glucose

Methyl-β-D-glucoside

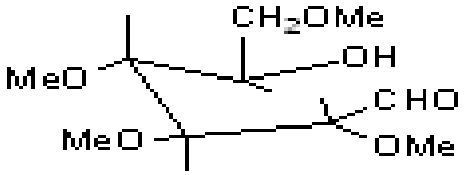
Determination of ring size cont.

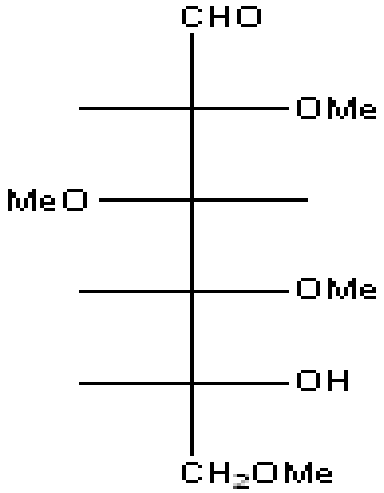


Methyl-β-2, 3, 4, 6-O- methyl-D-glucoside

Determination of ring size cont.

β-2, 3, 4, 6-O- methyl-D-glucoside



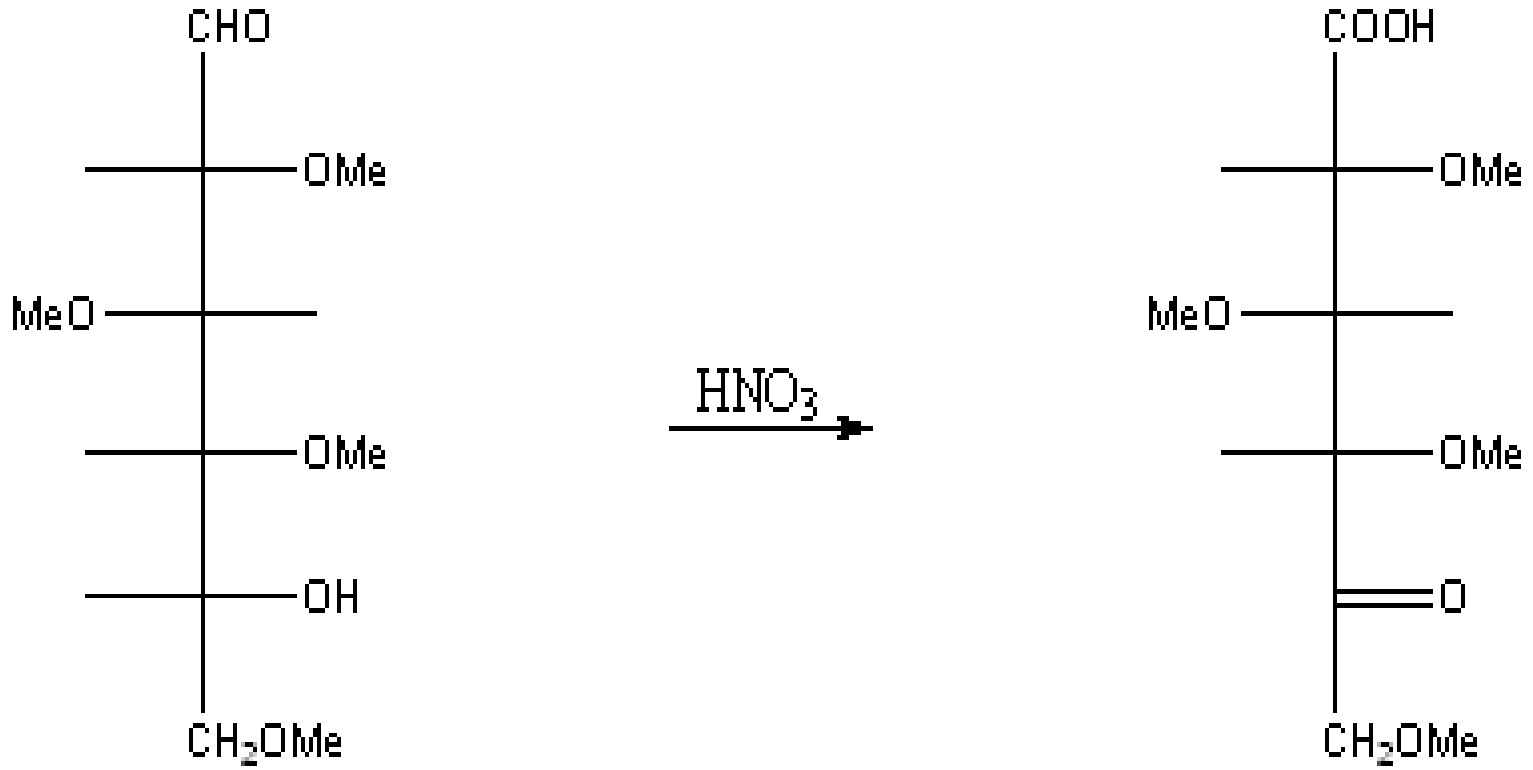


2, 3, 4, 6-O- methyl-D-glucoside (open chain form)

Determination of ring size cont.

- Vigorous oxidation by nitric acid of the tetra-O-mthyl-D-glucose will yield a ketocid:
  - the –CHO and the –OH group are oxidized
  - oxidation don't stop and the ketoacid is cleaved on one side or the other of the carbonyl carbon
  - oxidation usually yields a trimethoxyglutaric acid and dimethoxysuccinic acid

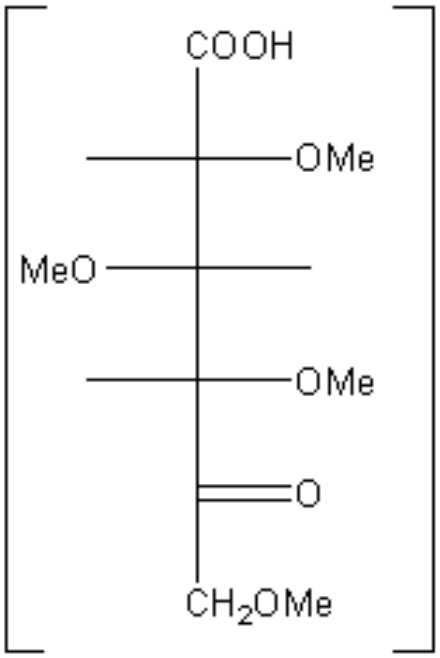
Determination of ring size cont.



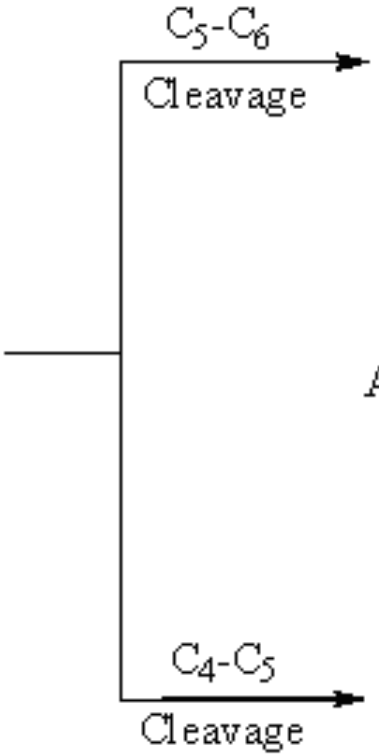
2, 3, 4, 6-O- methyl-D-glucoside

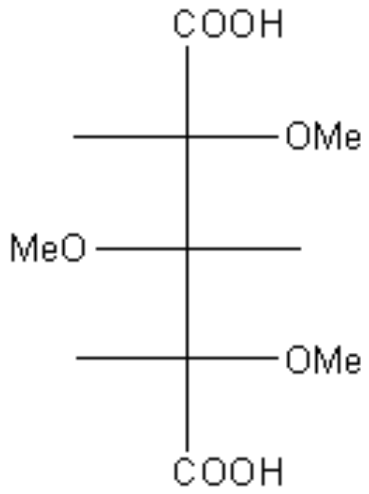
ketoacid

Determination of ring size cont.

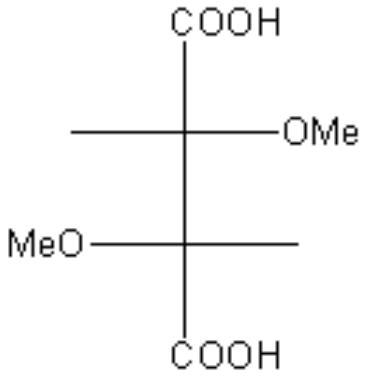


Ketoacid





A trimethoxyglutaric acid



A dimethoxysuccinic acid

Determination of ring size cont.

- A mixture of five-carbon and four-carbon acids could be formed only by cleavage on either side of C-5
- It must be C-5, therefore, that carries the carbonyl oxygen of the intermediate ketoacid and hence the free –OH group in the tetra-O-mthyl-D- glucose
  - Methyl-β-D-glucose must contain a six membered ring

Disaccharides

- Are made up of two monosaccharide units
- Include:
  - **(+)-Maltose** (malt sugar)
  - **(+)-Cellobiose**
  - **(+)-Lactose** (milk sugar) and
  - **(+)-Sucrose** (table sugar)

Disaccharides cont.

- As with the monosaccharides, focus will be given on the structures of these molecules:
  - Which monosaccharides make up the disaccharide?
  - How are they attached to each other?

Disaccharides cont.

(+)-Maltose

- Can be obtained, among other products, by hydrolysis of starch in aqueous acid
- Also formed in one stage of the fermentation of starch to ethyl alcohol
- Here the hydrolysis is catalized by the enzyme diastase, which is present in malt (sprouted barley)

Disaccharides cont.

- Facts from which the structure of maltose has been deduced:
  - Molecular formula = $C_{12}H_{22}O_{11}$
  - Reduce Tollen's and Fehling's reagents

    $\Rightarrow$ is reducing sugar

Disaccharides cont.

- Reacts with phenylhydrazine to yield an osazone
- Oxidized by bromine water to a monosaccharide acid (maltobionic acid)
- Exist as alpha ([α] = +168^0) and beta ([β] = +112^0) forms which undergo mutarotation in solution (equilibrium [α] = +136^0)

Disaccharides cont.

- All these facts indicate the same thing :
  - ⇒ (+)-Maltose contains a carbonyl group that exists in the hemiacetal form as in the monosaccharides
  - ⇒However, since
    - (a) the osazone contains only two phenylhydrazine residues, and

Disaccharides cont.

- (b)oxidation by bromine yields only a monocarboxylic acid,
- (+)-maltose contains only one such 'free' carbonyl group

Disaccharides cont.

- When hydrolyzed in aqueous acid, or when treated with the enzyme maltase (from yeast), (+)-maltose is completely converted in to D-(+)-glucose
  - $\Rightarrow$ (+)-Maltose is made up of two D-(+)-glucose units joined in some manner with the lose of one molecule of water

Disaccharides cont.

- Hydrolysis by acid to give a new reducing group (two reducing D-(+)-glucose molecules in place of one (+)-maltose molecule is a characteristic of glycosides
- Hydrolysis by the enzyme **maltase** is a characteristic of α-glycosides

Disaccharides cont.

- $\Rightarrow$ (+)-maltose contains two D-(+)-glucose units,
  - joined by an α-glycosidic linkage between the carbonyl groups of one D-(+)-glucose unit and an –OH group of the other
- $\Rightarrow$But which –OH group is involved, and what are the sizes of the rings in the two D-(+)-glucose units

Disaccharides cont.

- Treatment by bromine water coverts (+)-maltose into the monocarboxylic acid D-maltobionic acid
- Treatment of this acid with methylsulfate and sodium hydroxide yields octa-O-methyl-D-maltobionic acid
- Up on hydrolysis in acidic solution, the methylated acid yields two products:

Disaccharides cont.

- 2, 3, 5, 6-tetra-O-methyl-D-gluconic acid and
- 2, 3, 4, 6- tetra-O-methyl-D-glucose

- ⇒The –OH group on C-4 serves as the alcohol in the glycosidic formation
- ⇒Both halves of the molecule contain the six membered pyranose ring

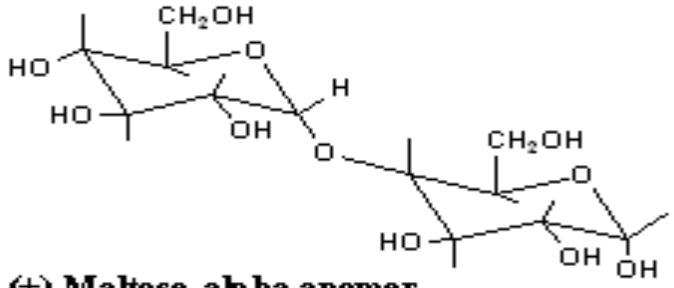
Disaccharides cont.

- Because:

1. Oxidation labels the free aldehyde group of glucose with –COOH
2. Methylation labels the free –OH group as $-OCH_3$ and
3. Upon hydrolysis, the absence of a methoxy group shows which-OH group were not free for methylation

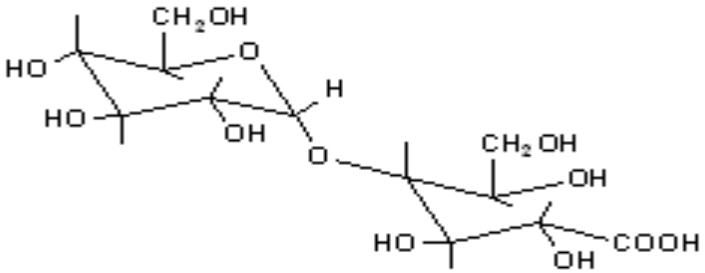
Disaccharides cont.

- ⇒The oxidized product 2, 3, 5, 6-tetra-O-methyl-D-gluconic acid must have arisen from the reducing (oxidizable) D-glucose unit
  - The presence of a free –OH group at C-4 shows that this position was not available for methylation at the maltobionic acid stage; hence it is the –OH at the C-4 that is tied up in the glucoside linkage at maltobionic acid and of (+)-maltose itself



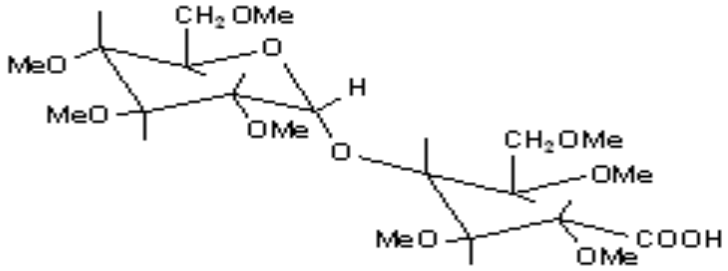
(+)-Maltose, alpha anomer

Br_2/H_2O **Oxidation**



D-Maltobionic acid, probably as a lactone

$Me_2SO_4/NaOH$ **Methylation**



Octa-O-methyl-D-maltobionic acid

(a) Oxidation and methylation

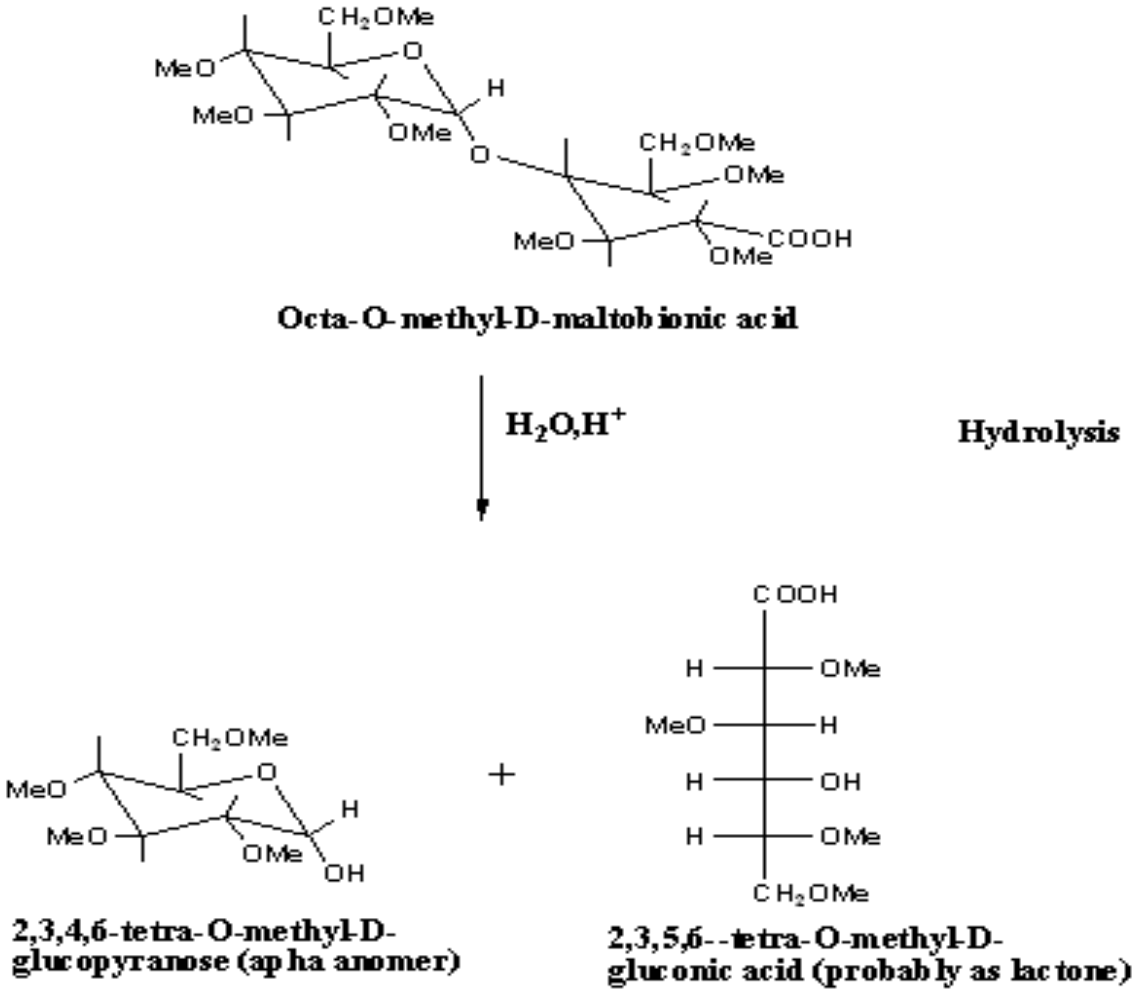


Figure-Sequence of (a) oxidation, methylation, and (b) hydrolysis-showing that (+)-maltose is 4-O-(α-D-glucopyranosyl)-D-glucopyranose

Disaccharides cont.

(+)-Cellobiose (obtained from cellulose)

- When cellulose (cotton fiber) is treated, for several days, with sulphuric acid and acetic anhydride, a combination of acetylation and hydrolysis takes place
  - ⇒Octaacetate of (+)-cellobiose is obtained
  - ⇒Alkaline hydrolysis of the octaacetate yields(+)-cellobiose

Disaccharides cont.

- Like (+)-matose, (+)-cellobiose
  - Has the molecular formula $C_{12}H22O_{11}$
  - Is a reducing sugar
  - Forms an osazone
  - Exist as an α and β forms that undergo mutarotation
  - Can be hydrolysed to two molecules of D-(+)-glucose

Disaccharides cont.

- The sequence of oxidation, methylation, and hydrolysis shows that it contains two pyranose ring and glucoside linkage to an –OH group at C-4
- (+)-Cellobiose differ from (+)-maltose only in one respect:
  - It is hydrolysed by the enzyme **emulsin** (from bitter almond) not by **maltase**
  - Emulsin is known to hydrolyse only β-glucoside linkage

Disaccharides cont.

✓ Conclusion:

- the structure of cellobiose differ from (+)-maltose only in the kind of glycoside linkage
- The D-(+)-glucose units are joined only by β- linkage in cellobiose than by α- linkage, which is the case in maltose

➢ Cellobiose is, therefore, **4-O-(β-D-Glucopyranosyl)-D-glucopyranose**

Disaccharides cont.

(+)-Lactose (milk sugar)

- Made up of 5% of human milk and of cow's milk
- Is obtained commercially as a by product of cheese manufacture, being found in the whey, the aqueous solution that remains after the milk proteins have been coagulated
  - Milk sours when lactose is converted to lactic acid (sour, like all acid) by bacterial action (eg *Lactobacillus bulgaricum*)

Disaccharides cont.

- **(+)-Lactose**
  - Has the molecular formula $C_{12}H_{22}O_{11}$
  - Is a reducing sugar
  - Forms an osazone
  - Exist as an α and β forms that undergo mutarotation

Disaccharides cont.

- **Acidic** hydrolysis or treatment with **emulsion** converts lactose into equal amount of D-(+)-glucose and D-(+)-galactose
  - $\Rightarrow$ (+)-Lactose is β-glucoside formed by the union of a molecule of D-(+)-glucose and a molecule of D-(+)-galactose
  - $\Rightarrow$ But is it a glucoside or a galactoside?

Disaccharides cont.

- Hydrolysis of lactosazone yields D-(+)-galactose and D-(+)-glucosazone
- Hydrolysis of lactobionic acid yields D-gluconic acid and D-(+)-galactose
  - $\Rightarrow$It is the D-(+)-glucose unit that contains the free aldehyde group and undergoes osazone formation or oxidation to the acid

Disaccharides cont.

- $\Rightarrow$ (+)-Lactose is thus substituted D-glucose in which a galactosyl unit is attached to one of the oxigens
- $\Rightarrow$It is a galactoside not a glucoside

Disaccharides cont.

(+)-Sucrose (table sugar)

- (+)-Sucrose is the common table sugar, obtained from sugar cane.

Disaccharides cont.

- (+)-Sucrose

1. Has the molecular formula $C_{12}H_{22}O_{11}$
2. Is a non-reducing sugar
3. Does not forms an osazone
4. Does not exist as an anomeric forms and
5. Does not undergo mutarotation

Disaccharides cont.

- Points 2-5 indicate that (+)-sucrose does not contain a free aldehyde or ketone group
- When (+)-sucrose is hydrolyzed by dilute aqueous acidic or by the action of the enzyme invertase (from yeast), it yield two equal amounts of D-(+) glucose and D-(-)-fructose.

Disaccharides cont.

- ⇒This hydrolysis is accompanied by changes in the sign of rotation from positive to negative
- ⇒It is, therefore, often called the inversion of (+)-sucrose, and the levorotatory mixture of D-(+) glucose and D-(-)-fructose is called ***invert sugar***

Disaccharides cont.

- ⇒Honey is mostly invert sugar, the bees supply the invertase
  - (+)-sucrose has [α] = +66.5°
  - D-(+) glucose has [α] = +52.7°
  - D-(-)-fructose has [α] = -92.4°

Disaccharides cont.

- Giving a net negative value for the [α] of the mixture (invert sugar)
  - $\Rightarrow$Because of their opposite rotations and their importance as components of (+)-sucrose, D-(+) glucose and D-(-)-fructose are commonly called *dextrose* and *laevulose*

Disaccharides cont.

- (+)-Sucrose is made up of a D- glucose and a D-fructose units and
- since there is no free carbonyl group, it must be both a D-glucoside and a D-fructoside
  - The two hexoses units are evidently joined by a glucoside linkage between C-1 of glucose and C-2 of fructose, for only in this way can the single link between the two units effectively block both carbonyl groups

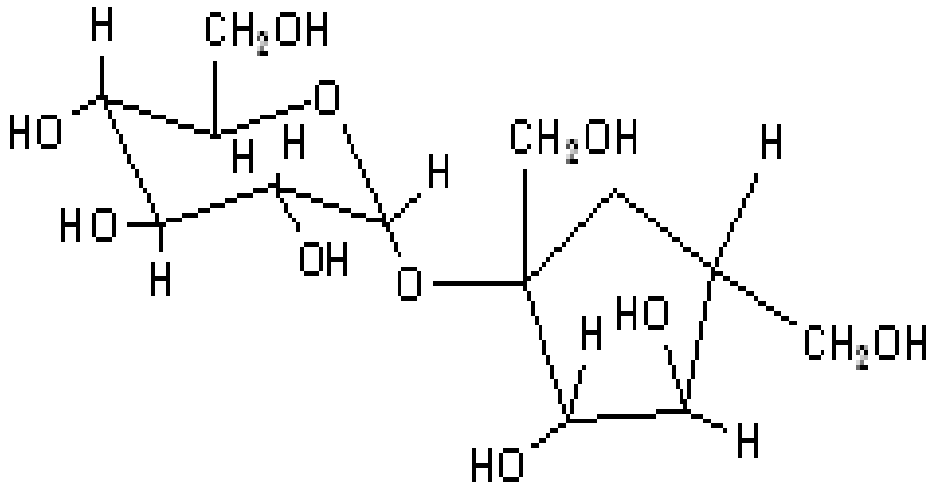
Disaccharides cont.

- Determination of the stereochemistry of the D-glucoside and D-fructoside is complicated by the fact that both linkage are hydrolyzed at the same time
- X-ray studies and synthesis of (+)-sucrose indicate that (+)-sucrose is a β-D-fructoside and an α-D-glucoside

Disaccharides cont.

- Methylation and hydrolysis shows that (+)-sucrose contains a D-glucopyranose and a D-fructofuranose units
- (+)-sucrose is named equally well as **either**
  - α-D-glucopyranosyl β-D-fructofuranoside **or**
  - β-D-fructofuranosyl α-D-glucopyranoside

Disaccharides cont.



(+)-sucrose

α-D-glucopyranosyl β-D-fructofuranoside

β-D-fructofuranosyl α-D-glucopyranoside

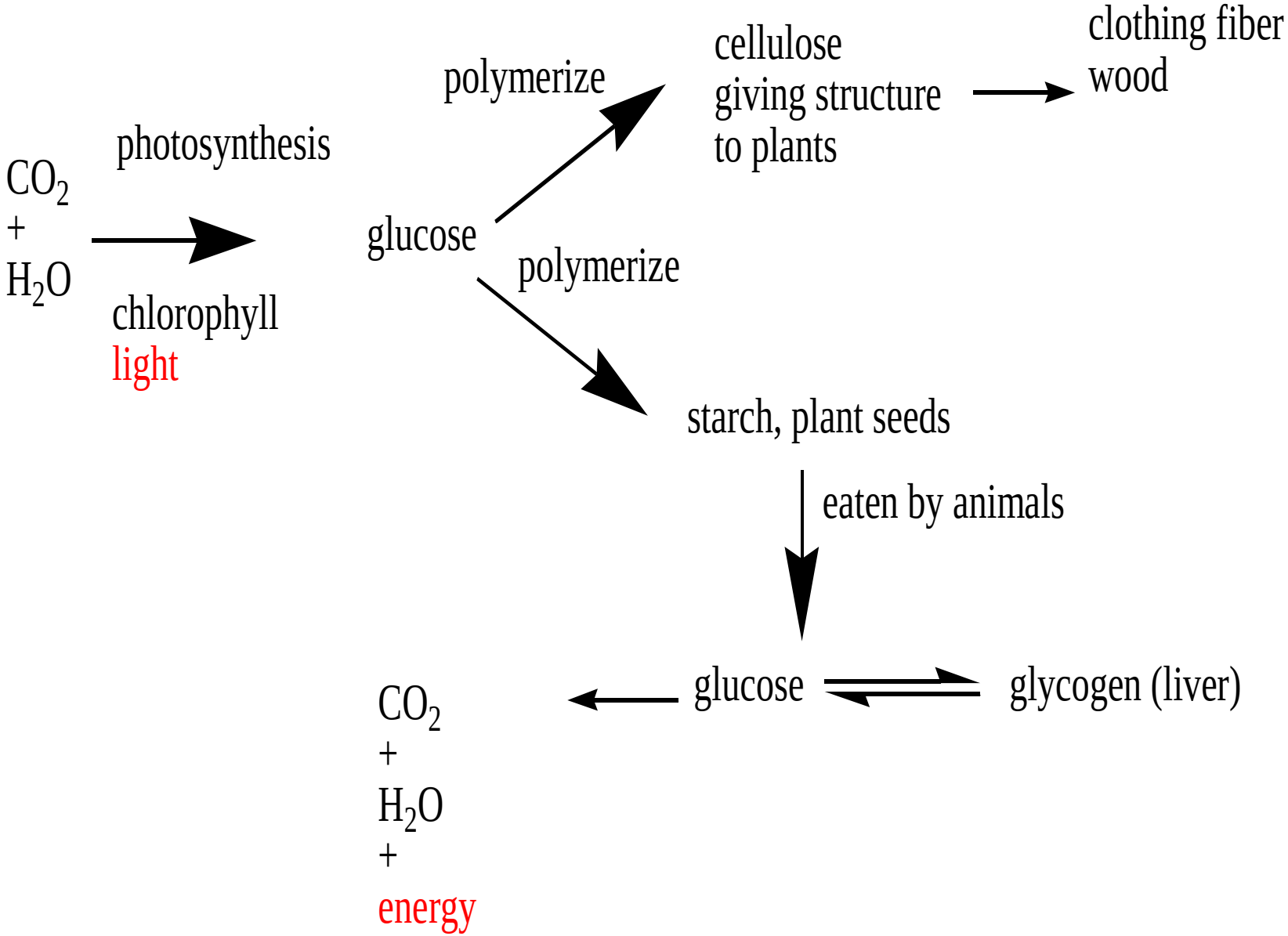
(no anomers, non-mutarotating)

Polysaccharides (starch and cellulose)

- Polysaccharides are made up of many- hundreds or even thousands-monosaccharide units per molecule
- The units are held together by glycoside linkage, which is broken by hydrolysis
- Are naturally occurring polymers, which can be considered as derived from aldoses or ketoses by polymerization with lose of water

Polysaccharides cont.

- By far the most important polysaccharides are cellulose and starch; both are:
  - Produced in plants from CO_2 and H_2O by the process of photosynthesis
  - Made up of D-(+)- glucose units


CO_2
+
H_2O
photosynthesis
chlorophyll
light
glucose
polymerize
cellulose
giving structure
to plants
clothing fiber
wood
polymerize
starch, plant seeds
eaten by animals
glucose
glycogen (liver)
CO_2
+
H_2O
+
energy

Polysaccharides cont.

Starch

- Make up the reserve food supply of plants
- Occurs chiefly in seeds
- Is more water soluble than cellulose and more easily hydrolyzed
- Occurs as granules whose size and shape are characteristic of the plant from which the starch is obtained

Polysaccharides cont.

- Intact starch granules are insoluble in cold water,
  - ✓but if the outer membrane has been broken by grinding,

    the granules swell, in cold water, and forms a gel

Polysaccharides cont.

- When the intact granule of starch are treated with warm water,
  - a soluble portion of the starch diffuses through the granule wall;
  - in hot water the granules swell to such an extent that they burst

Polysaccharides cont.

- In general, starch contains about
  - 20% of water soluble fraction called **amylose** and
  - 80% of water insoluble fraction called **amylopectin**
- Up on treatment with acid or under the influence of enzymes,

Polysaccharides cont.

- the components of starch are hydrolyzed progressively to dextrin (a mixture of low mol. weight polysaccharides, (+)-maltose and finally to D-(+)-glucose
- thus, both amylose and amylopecin are made up of D-(+)-glucose units, but differ in molecular size and shape

Polysaccharides cont.

Structure of amylose - End group analysis

- Hydrolysis of amylose produces
  - (+)-maltose as the only disaccharide and
  - D-(+)-glucose as the only monosaccharide
    - ⇒Amylose is made up of chains of many D-(+)-glucose units

Polysaccharides cont.

- ⇒Each unit is joined by an α-glycoside linkage to C-4 of the next one because,
  - If there was β-linkage, cellobiose would have also been produced during hydrolysis

- **How many of D-(+)-glucose molecules are there in a molecule of amylose?**

Polysaccharides cont.

- **What is the shape of these large molecules?**
- When amylose is methylated and hydrolyzed,
  - 2,3,6-tri-O-methyl-D-glucose is obtained (expected)
  - A little (about 0.2-0.4%) of 2,3,4,6- tetra-O-methyl-D-glucose is also obtained (also expected unless cyclic)

Polysaccharides cont.

- ⇒Each glucose unit, in amylase, is attached to two other D-glucose units,
  - One through C-1 and
  - the other through C-4
  - with C-5 in every unit tied up in the pyranose ring

Polysaccharides cont.

- ⇒Therefore, free –OH groups at C-2, C-3, and C-6 are available for methylation
  - But this is not the case for every D-glucose unit unless amylose is cyclic, it must have two ends
  - At one end, there should be a D-glucose unit that have free –OH on C-4

Polysaccharides cont.

- This last D-glucose unit must undergo methylation at four –OH groups and on hydrolysis should give a molecule of 2, 3, 4, 6- tetra-O-methyl-D-glucose

- ⇒Thus each molecule of completely methylated amylose that is hydrolyzed should yield one molecule of 2, 3, 4, 6-tetra-O-methyl-D-glucose;

Polysaccharides cont.

- From the number of tri-O-methyl-D-glucose formed along with each molecule of the tetra-O-methyl-D-glucose compound the length of the amylose can be calculated

Polysaccharides cont.

Structure of amylopectin

- Insoluble fraction of starch
- Amylopectin is hydrolyzed to a single disaccharide, (+)-maltose
- The sequence of methylation and hydrolysis yields chiefly of 2, 3, 6-tri-O-methyl-D-glucose
  - It is thus made up of chains of D-glucose units, each unit joined by an α-glycosidic linkage to C-4 of the next one

Polysaccharides cont.

- M. weight determination of physical methods show that there are up to a million D-glucose units per molecule
- Yet hydrolysis of methylated amylopectin gives as high as 5% of 2,3,4,6-tetra-O-methyl-D-glucose, indicating only 20 units per chain
  - **How?**

Polysaccharides cont.

- Along with the trimethyl and tetramethyl compound, hydrolysis yields 2,3-Di-O-mthyl-D-glucose and in an amount nearly equal to that of the tetramethyl derivative

Polysaccharides cont.

- ⇒Amylopectin has a highly branched structure consisting of several hundred short chains of about 20-25 D-glucose units each
- ⇒One end of each of these chains is joined through C-1 to a C-6 on the next chain

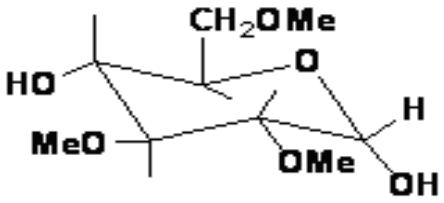
Polysaccharides cont.

- Thus, amylopectin

- Is branched, insoluble fraction of starch
- Is Polymer of α-D-Glucose units with (1⟶4) linkage in the main chain and
- In addition to the (1⟶4) linkage are (1⟶6) linkage at branching

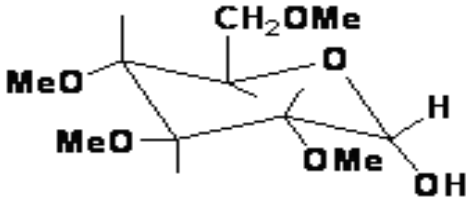
Methylated Amylopectin

↓ **Hydrolysis**



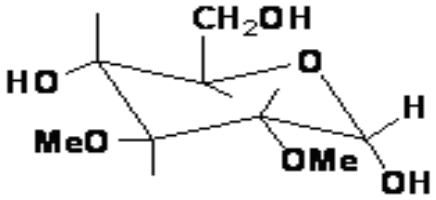
2,3,6-tri-O-methyl-D-glucose
~90%

+



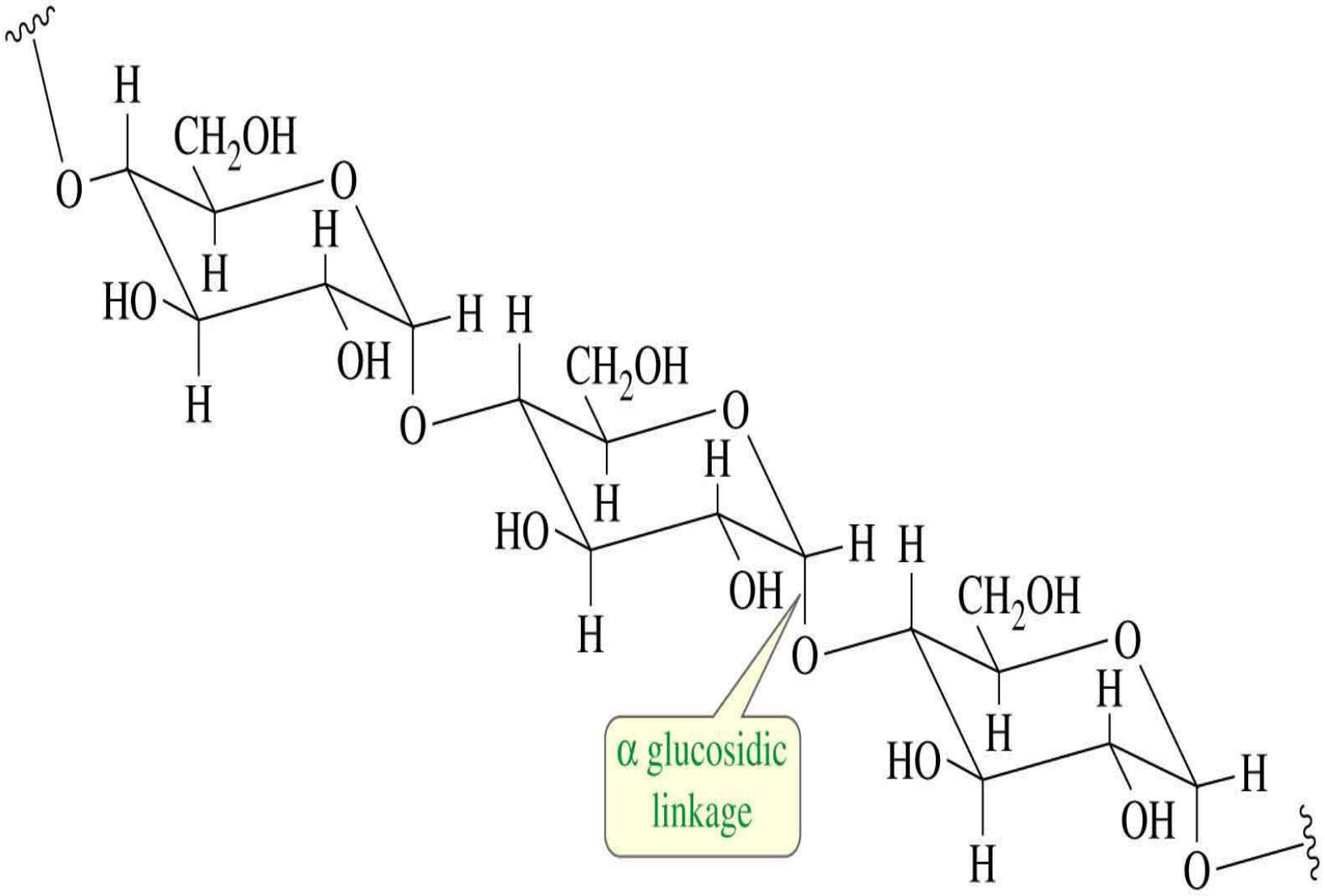
2,3,4,6-tetra-O-methyl-D-glucose
~5%

+

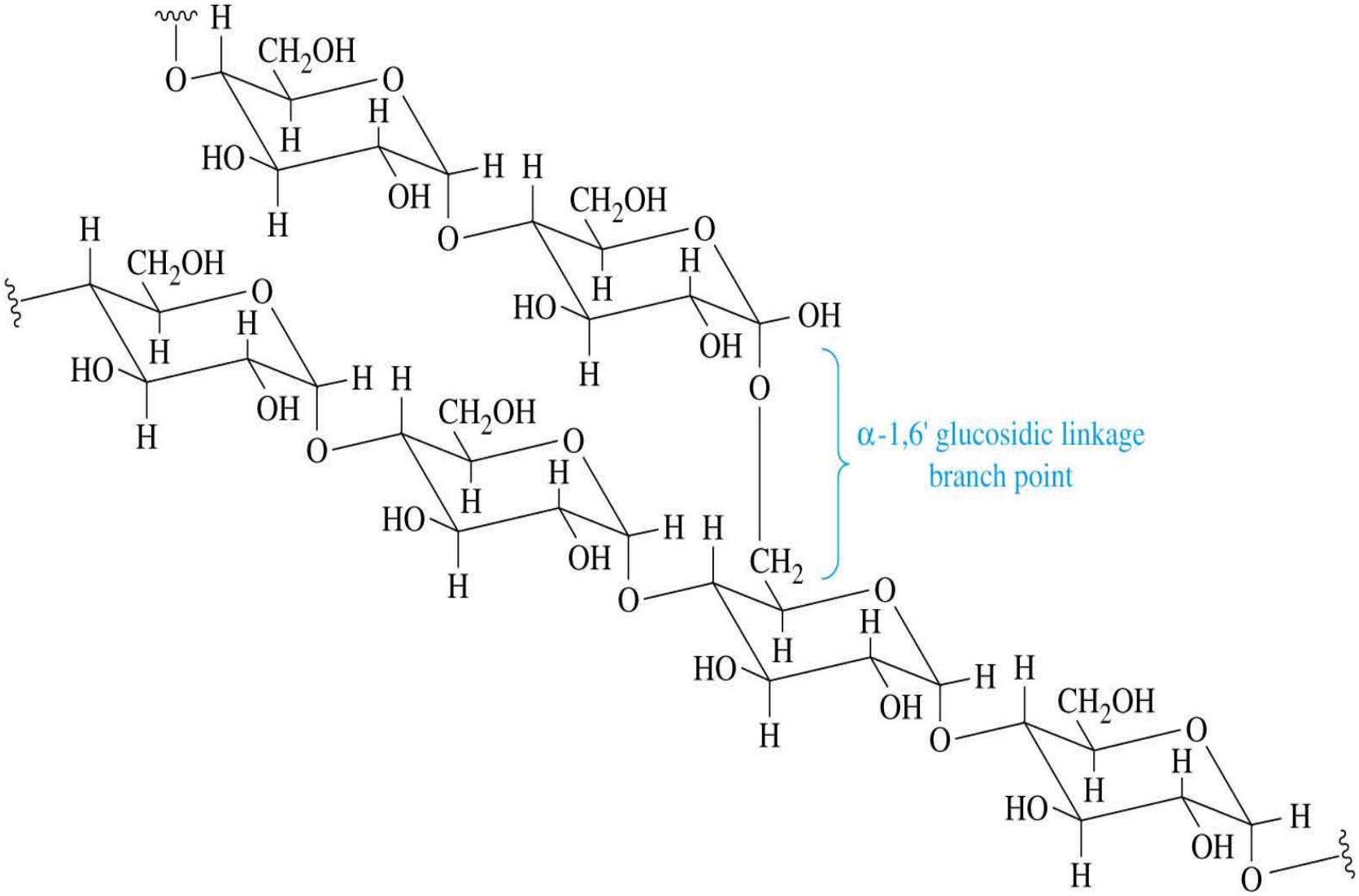


2,3-Di-O-methyl-D-glucose
~5%

Polysaccharides cont.



Polysaccharides cont.

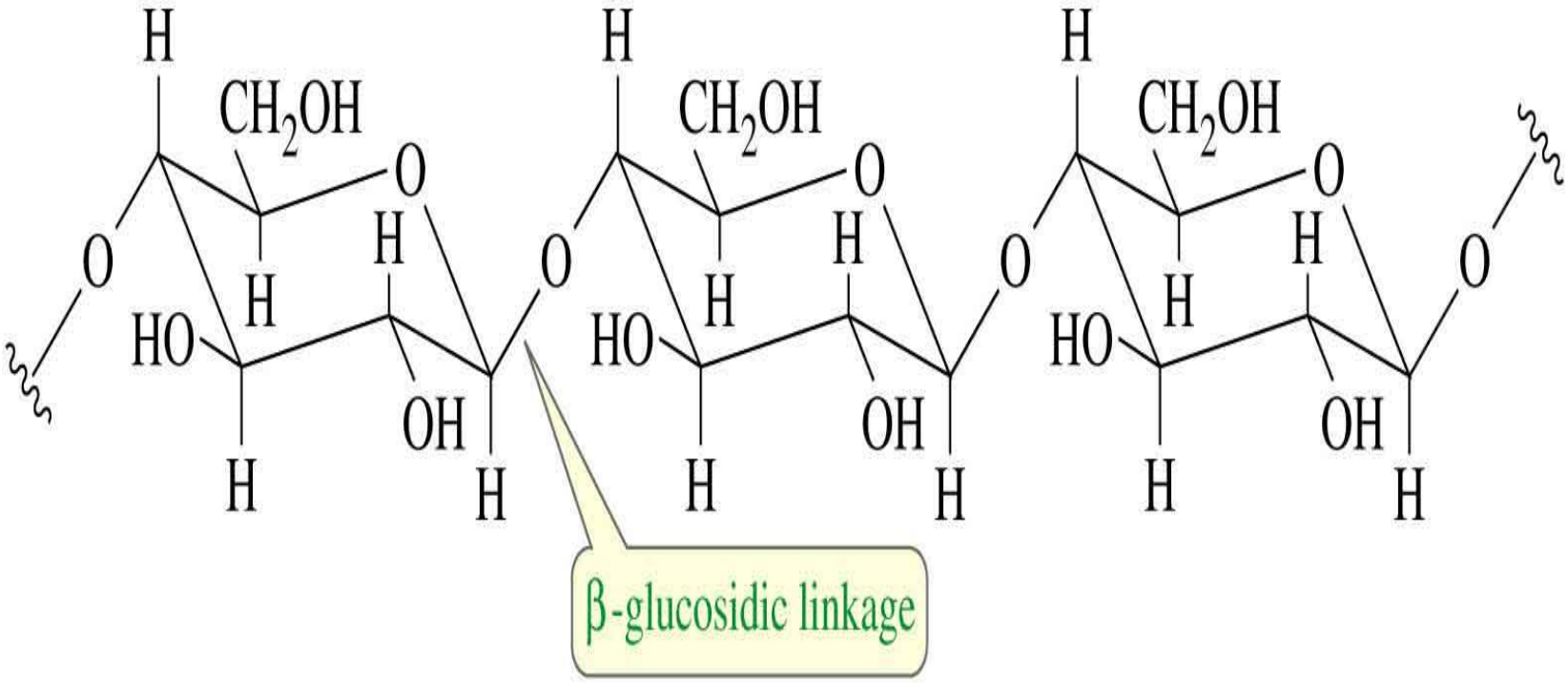


Polysaccharides cont.

Cellulose

- Most abundant of all carbohydrates
  - Cotton flax: 97-99% cellulose
  - Wood: ~ 50% cellulose
- Polymer of β-D-glucose attached by β(1⟶4) linkages
  - Yields glucose upon complete hydrolysis
  - Partial hydrolysis yields cellobiose

Polysaccharides cont.



End of Topic